PCT

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ^{6} : G01N 33/53	A2	(11) International Publication Number: **WO 98/45704**
		(43) International Publication Date: 15 October 1998 (15.10.98)

(21) International Application Number: PCT/DK98/00145

(22) International Filing Date: 7 April 1998 (07.04.98)

(30) Priority Data:
0392/97   7 April 1997 (07.04.97)   DK

(71) Applicant *(for all designated States except US)*: NOVO NORDISK A/S [DK/DK]; Novo Allé, DK–2880 Bagsvaerd (DK).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: THASTRUP, Ole [DK/DK]; Birkevej 37, DK–3460 Birkerød (DK). PETERSEN BJØRN, Sara [DK/DK]; Klampenborgvej 102, DK–2800 Lyngby (DK). TULLIN, Søren [DK/DK]; Karl Gjellerups Alle 18, DK–2860 Søborg (DK). KASPER, Almholt [DK/DK]; Eigilsgade 32, 4. tv, DK–2300 København S (DK). SCUDDER, Kurt [US/DK]; Lavendelhaven 70, DK–2830 Virum (DK).

(74) Common Representative: NOVO NORDISK A/S; attn. Lars Kellberg, Novo Allé, DK–2880 Bagsværd (DK).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
Without international search report and to be republished upon receipt of that report.

(54) Title: A METHOD FOR EXTRACTING QUANTITATIVE INFORMATION RELATING TO AN INFLUENCE ON A CELLULAR RESPONSE

(57) Abstract

Cells are genetically modified to expresss a luminophore, e.g., a modified (F64L, S65T, Y66H) Green Fluorescent Protein (GFP, EGFP) coupled to a component of an intracellular signalling pathway such as a transcription factor, a cGMP– or cAMP–dependent protein kinase, a cyclin–, calmodulin– or phospholipid–dependent or mitogen–activated serine/threonin protein kinase, a tyrosine protein kinase, or a protein phosphatase (e.g. PKA, PKC, Erk, Smad, VASP, actin, p38, Jnk1, PKG, IkappaB, CDK2, Grk5, Zap70, p85, protein–tyrosine phosphatase 1C, Stat5, NFAT, NFkappaB, RhoA, PKB). An influence modulates the intracellular signalling pathway in such a way that the luminophore is being redistributed or translocated with the component in living cells in a manner experimentally determined to be correlated to the degree of the influence. Measurement of redistribution is performed by recording of light intensity, fluorescence lifetime, polarization, wavelength shift, resonance energy transfer, or other properties by an apparatus consisting of e.g. a fluorescence microscope and a CCD camera. Data stored as digital images are processed to numbers representing the degree of redistribution. The method can be used as a screening program for identifying a compound that modulates a component and is capable of treating a disease related to the function of the component.

1

A METHOD for extracting quantitative information relating to an influence on a cellular response

FIELD OF INVENTION

5   The present invention relates to a method and tools for extracting quantitative information relating to an influence, on a cellular response, in particular an influence caused by contacting or incubating the cell with a substance influencing a cellular response, where the cellular response is manifested in redistribution of at least one component in the cell. In particular, the invention relates to a method for extracting quantitative information relating to an influen-

10 ce on an intracellular pathway involving redistribution of at least one component associated with the pathway. The method of the invention may be used as a very efficient procedure for testing or discovering the influence of a substance on a physiological process, for example in connection with screening for new drugs, testing of substances for toxicity, identifying drug targets for known or novel drugs Other valuable uses of the method and technology of the

15 invention will be apparent to the skilled person on the basis of the following disclosure. In a particular embodiment of the invention, the present invention relates to a method of detecting intracellular translocation or redistribution of biologically active polypeptides, preferably an enzyme, affecting intracellular processes, and a DNA construct and a cell for use in the method.

20

BACKGROUND OF THE INVENTION

Intracellular pathways are tightly regulated by a cascade of components that undergo modulation in a temporally and spatially characteristic manner. Several disease states can be attributed to altered activity of individual signalling components (i.e. protein kinases, pro-

25 tein phosphatases, transcription factors). These components therefore render themselves as attractive targets for therapeutic intervention.

Protein kinases and phosphatases are well described components of several intracellular signalling pathways. The catalytic activity of protein kinases and phosphatases are assumed to play a role in virtually all regulatable cellular processes. Although the involvement of pro-

30 tein kinases in cellular signalling and regulation have been subjected to extensive studies, detailed knowledge on e.g. the exact timing and spatial characteristics of signalling events is often difficult to obtain due to lack of a convenient technology.

SUBSTITUTE SHEET (RULE 26)

Novel ways of monitoring specific modulation of intracellular pathways in intact, living cells is assumed to provide new opportunities in drug discovery, functional genomics, toxicology, patient monitoring etc.

The spatial orchestration of protein kinase activity is likely to be essential for the high degree
5   of specificity of individual protein kinases. The phosphorylation mediated by protein kinases is balanced by phosphatase activity. Also within the family of phosphatases translocation has been observed, e.g. translocation of PTP2C to membrane ruffles [(Cossette et al.1996)], and likewise is likely to be indicative of phosphatase activity.

Protein kinases often show a specific intracellular distribution before, during and after activa-
10   tion. Monitoring the translocation processes and/or redistribution of individual protein kinases or subunits thereof is thus likely to be indicative of their functional activity. A connection between translocation and catalytic activation has been shown for protein kinases like the diacyl glycerol (DAG)-dependent protein kinase C (PKC), the cAMP-dependent protein kinase (PKA) [(DeBernardi et al.1996)] and the mitogen-activated-protein kinase Erk-1 [(Sano et
15   al.1995)].

Commonly used methods of detection of intracellular localisation/activity of protein kinases and phosphatases are immunoprecipitation, Western blotting and immunocytochemical detection.

Taking the family of diacyl glycerol (DAG)-dependent protein kinase Cs (PKCs) as an exam-
20   ple, it has been shown that individual PKC isoforms that are distributed among different tissues and cells have different activator requirements and undergo differential translocation in response to activation. Catalytically inactive DAG-dependent PKCs are generally distributed throughout the cytoplasm, whereas they upon activation translocate to become associated with different cellular components, e.g. plasma membrane [(Farese, 1992),(Fulop Jr. et
25   al.1995)] nucleus [(Khalil et al.1992)], cytoskeleton [(Blobe et al.1996)]. The translocation phenomenon being indicative of PKC activation has been monitored using different approaches: a) immunocytochemistry where the localisation of individual isoforms can be detected after permeabilisation and fixation of the cells [(Khalil et al.1992)]; and b) tagging all DAG-dependent PKC isoforms with a fluorescently labelled phorbol myristate acetate (PMA)
30   [(Godson et al.1996)]; and c) chemical tagging PKC b1 with the fluorophore Cy3 [(Bastiaens & Jovin 1996)] and d) genetic tagging of PKCα ([Schmidt et al. 1997]) and of PKCγ and PKC ε ([Sakai et al. 1996]). The first method does not provide dynamic information whereas the latter methods will. Tagging PKC with fluorescently labelled phorbol myristate acetate cannot

distinguish between different DAG-dependent isoforms of PKC but will label and show movement of all isoforms. Chemical and genetic labelling of specific DAG-dependent PKCs confirmed that they in an isoform specific manner upon activation move to cell periphery or nucleus.

5 In an alternative method, protein kinase A activity has been measured in living cells by chemical labelling one of the kinase's subunit (Adams *et al.*1991). The basis of the methodology is that the regulatory and catalytic subunit of purified protein kinase A is labelled with fluorescein and rhodamine, respectively. At low cAMP levels protein kinase A is assembled in a heterotetrameric form which enables fluorescence resonance energy transfer between 10 the two fluorescent dyes. Activation of protein kinase A leads to dissociation of the complex, thereby eliminating the energy transfer. A disadvantage of this technology is that the labelled protein kinase A has to be microinjected into the cells of interest. This highly invasive technique is cumbersome and not applicable to large scale screening of biologically active substances. A further disadvantage of this technique as compared to the presented invention is 15 that the labelled protein kinase A cannot be inserted into organisms/animals as a transgene.

Recently it was discovered that Green Fluorescent Protein (GFP) expressed in many different cell types, including mammalian cells, became highly fluorescent [(Chalfie *et al.*1994)]. WO95/07463 describes a cell capable of expressing GFP and a method for detecting a protein of interest in a cell based on introducing into a cell a DNA molecule having DNA se- 20 quence encoding the protein of interest linked to DNA sequence encoding a GFP such that the protein produced by the DNA molecule will have the protein of interest fused to the GFP, then culturing the cells in conditions permitting expression of the fused protein and detecting the location of the fluorescence in the cell, thereby localizing the protein of interest in the cell. However, examples of such fused proteins are not provided, and the use of fusion pro- 25 teins with GFP for detection or quantitation of translocation or redistribution of biologically active polypeptides affecting intracellular processes upon activation, such as proteins involved in signalling pathways, e.g. protein kinases or phosphatases, has not been suggested. WO 95/07463 further describes cells useful for the detection of molecules, such as hormones or heavy metals, in a biological sample, by operatively linking a regulatory ele- 30 ment of the gene which is affected by the molecule of interest to a GFP, the presence of the molecules will affect the regulatory element which in turn will affect the expression of the GFP. In this way the gene encoding GFP is used as a reporter gene in a cell which is constructed for monitoring the presence of a specific molecular identity.

4

Green Fluorescent Protein has been used in an assay for the detection of translocation of the glucocorticoid receptor (GR) [Carey, KL et al., The Journal of Cell Biology, Vol. 133, No. 5, p. 985-996 (1996)]. A GR-S65TGFP fusion has been used to study the mechanisms in-volved in translocation of the glucocorticoid receptor (GR) in response to the agonist dex-

5   amethasone from the cytosol, where it is present in the absence of a ligand, through the nu-clear pore to the nucleus where it remains after ligand binding. The use of a GR-GFP fusion enables real-time imaging and quantitation of nuclear/cytoplasmic ratios of the fluorescence signal.

Many currently used screening programmes designed to find compounds that affect protein

10   kinase activity are based on measurements of kinase phosphorylation of artificial or natural substrates, receptor binding and/or reporter gene expression.

DISCLOSURE OF THE INVENTION

The present invention provides an important new dimension in the investigation of cellular

15   systems involving redistribution in that the invention provides quantification of the redistribu-tion responses or events caused by an influence, typically contact with a chemical substance or mixture of chemical substances, but also changes in the physical environment. The quan-tification makes it possible to set up meaningful relationships, expressed numerically, or as curves or graphs, between the influences (or the degree of influences) on cellular systems

20   and the redistribution response. This is highly advantageous because, as has been found, the quantification can be achieved in both a fast and reproducible manner, and - what is per-haps even more important - the systems which become quantifiable utilizing the method of the invention are systems from which enormous amounts of new information and insight can be derived.

25   The present screening assays have the distinct advantage over other screening assays, e.g., receptor binding assays, enzymatic assays, and reporter gene assays, in providing a system in which biologically active substances with completely novel modes of action, e.g. inhibition or promotion of redistribution/translocation of a biologically active polypeptide as a way of regulating its action rather than inhibition/activation of enzymatic activity, can be iden-

30   tified in a way that insures very high selectivity to the particular isoform of the biologically ac-tive polypeptide and further development of compound selectivity versus other isoforms of

5

the same biologically active polypeptide or other components of the same signalling pathway.

In its broadest aspect, the invention relates to a method for extracting quantitative information relating to an influence on a cellular response, the method comprising recording variation,

5   caused by the influence on a mechanically intact living cell or mechanically intact living cells, in spatially distributed light emitted from a luminophore, the luminophore being present in the cell or cells and being capable of being redistributed in a manner which is related with the degree of the influence, and/or of being modulated by a component which is capable of being redistributed in a manner which is related to the degree of the influence, the association

10   resulting in a modulation of the luminescence characteristics of the luminophore, detecting and recording the spatially distributed light from the luminophore, and processing the recorded variation in the spatially distributed light to provide quantitative information correlating the spatial distribution or change in the spatial distribution to the degree of the influence. In a preferred embodiment of the invention the luminophore, which is present in the cell or cells,

15   is capable of being redistributed by modulation of an intracellular pathway, in a manner which is related to the redistribution of at least one component of the intracellular pathway. In another preferred embodiment of the invention, the luminophore is a fluorophore.

The cells

20   In the invention the cell and/or cells are mechanically intact and alive throughout the experiment. In another embodiment of the invention, the cell or cells is/are fixed at a point in time after the application of the influence at which the response has been predetermined to be significant, and the recording is made at an arbitrary later time.

The mechanically intact living cell or cells could be selected from the group consisting of

25   fungal cell or cells, such as a yeast cell or cells; invertebrate cell or cells including insect cell or cells; and vertebrate cell or cells, such as mammalian cell or cells. This cell or these cells is/are incubated at a temperature of 30°C or above, preferably at a temperature of from 32°C to 39°C, more preferably at a temperature of from 35°C to 38°C, and most preferably at a temperature of about 37°C during the time period over which the influence is observed. In

30   one aspect of the invention the mechanically intact living cell is part of a matrix of identical or non-identical cells.

6

A cell used in the present invention should contain a nucleic acid construct encoding a fusion polypeptide as defined herein and be capable of expressing the sequence encoded by the construct. The cell is a eukaryotic cell selected from the group consisting of fungal cells, such as yeast cells; invertebrate cells including insect cells; vertebrate cells such as mam-

5   malian cells. The preferred cells are mammalian cells.

In another aspect of the invention the cells could be from an organism carrying in at least one of its component cells a nucleic acid sequence encoding a fusion polypeptide as defined herein and be capable of expressing said nucleic acid sequence. The organism is selected from the group consisting of unicellular and multicellular organisms, such as a mammal.

10

The luminophore

The luminophore is the component which allows the redistribution to be visualised and/or recorded by emitting light in a spatial distribution related to the degree of influence. In one embodiment of the invention, the luminophore is capable of being redistributed in a manner

15   which is physiologically relevant to the degree of the influence. In another embodiment, the luminophore is capable of associating with a component which is capable of being redistributed in a manner which is physiologically relevant to the degree of the influence. In another embodiment, the luminophore correlation between the redistribution of the luminophore and the degree of the influence could be determined experimentally. In a preferred aspect of the

20   invention, the luminophore is capable of being redistributed in substantially the same manner as the at least one component of an intracellular pathway. In yet another embodiment of the invention, the luminophore is capable of being quenched upon spatial association with a component which is redistributed by modulation of the pathway, the quenching being measured as a change in the intensity of the luminescence.

25   The luminophore could be a fluorophore. In a preferred embodiment of the invention, the luminophore could be a polypeptide encoded by and expressed from a nucleotide sequence harboured in the cell or cells. The luminophore could be a hybrid polypeptide comprising a fusion of at least a portion of each of two polypeptides one of which comprises a luminescent polypeptide and the other one of which comprises a biologically active polypeptide, as defi-

30   ned herein.

The luminescent polypeptide could be a GFP as defined herein or could be selected from the group consisting of green fluorescent proteins having the F64L mutation as defined herein

SUBSTITUTE SHEET (RULE 26)

such as F64L-GFP, F64L-Y66H-GFP, F64L-S65T-GFP, and EGFP. The GFP could be N- or C-terminally tagged, optionally via a peptide linker, to the biologically active polypeptide or a part or a subunit thereof. The fluorescent probe could be a component of a intracellular signalling pathway. The probe is coded for by a nucleic acid construct.

5   The pathway of investigation in the present invention could be an intracellular signalling pathway.

The influence

In a preferred embodiment of the invention, the influence could be contact between the me-
10   chanically intact living cell or the group of mechanically intact living cells with a chemical substance and/or incubation of the mechanically intact living cell or the group of mechanically intact living cells with a chemical substance. The influence will modulate the intracellular processes. In one aspect the modulation could be an activation of the intracellular processes. In another aspect the modulation could be an deactivation of the intracellular processes.
15   In yet another aspect, the influence could inhibit or promote the redistribution without directly affecting the metabolic activity of the component of the intracellular processes.

In one embodiment the invention is used as a basis for a screening program, where the effect of unknown influences such as a compound library, can be compared to influence of known reference compounds under standardised conditions.

20

The recording

In addition to the intensity, there are several parameters of fluorescence or luminescence which can be modulated by the effect of the influence on the underlying cellular phenomena, and can therefore be used in the invention. Some examples are resonance energy transfer,
25   fluorescence lifetime, polarisation, wavelength shift. Each of these methods requires a particular kind of filter in the emission light path to select the component of the light desired and reject other components. The recording of property of light could be in the form of an ordered array of values such as a CCD array or a vacuum tube device such as a vidicon tube.

In one embodiment of the invention, the spatially distributed light emitted by a luminophore
30   could be detected by a change in the resonance energy transfer between the luminophore and another luminescent entity capable of delivering energy to the luminophore, each of

which has been selected or engineered to become part of, bound to or associated with particular components of the intracellular pathway. In this embodiment, either the luminophore or the luminescent entity capable of delivering energy to the luminophore undergoes redistribution in response to an influence. The resonance energy transfer would be measured as a

5   change in the intensity of emission from the luminophore, preferably sensed by a single channel photodetector which responds only to the average intensity of the luminophore in a non-spatially resolved fashion.

In one embodiment of the invention, the recording of the spatially distributed light could be made at a single point in time after the application of the influence. In another embodiment,

10   the recording could be made at two points in time, one point being before, and the other point being after the application of the influence. The result or variation is determined from the change in fluorescence compared to the fluorescence measured prior to the influence or modulation. In another embodiment of the invention, the recording could be performed at a series of points in time, in which the application of the influence occurs at some time after

15   the first time point in the series of recordings, the recording being performed, e.g., with a predetermined time spacing of from 0.1 seconds to 1 hour, preferably from 1 to 60 seconds, more preferably from 1 to 30 seconds, in particular from 1 to 10 seconds, over a time span of from 1 second to 12 hours, such as from 10 seconds to 12 hours, e.g., from 10 seconds to one hour, such as from 60 seconds to 30 minutes or 20 minutes. The result or variation is

20   determined from the change in fluorescence over time. The result or variation could also be determined as a change in the spatial distribution of the fluorescence over time.

Apparatus

The recording of spatially distributed luminescence emitted from the luminophore is perfor-

25   med by an apparatus for measuring the distribution of fluorescence in the cell or cells, and thereby any change in the distribution of fluorescence in the cell or cells, which includes at a minimum the following component parts: (a) a light source, (b) a method for selecting the wavelength(s) of light from the source which will excite the fluorescence of the protein, (c) a device which can rapidly block or pass the excitation light into the rest of the system, (d) a

30   series of optical elements for conveying the excitation light to the specimen, collecting the emitted fluorescence in a spatially resolved fashion, and forming an image from this fluorescence emission, (e) a bench or stand which holds the container of the cells being measured in a predetermined geometry with respect to the series of optical elements, (f) a detector to

record the spatially resolved fluorescence in the form of an image, (g) a computer or electronic system and associated software to acquire and store the recorded images, and to compute the degree of redistribution from the recorded images.

In a preferred embodiment of the invention the apparatus system is automated. In one em-
5   bodiment the components in d and e mentioned above comprise a fluorescence microscope. In one embodiment the component in f mentioned above is a CCD camera.

In one embodiment the image is formed and recorded by an optical scanning system.

In one embodiment a liquid addition system is used to add a known or unknown compound to any or all of the cells in the cell holder at a time determined in advance. Preferably, the
10   liquid addition system is under the control of the computer or electronic system. Such an automated system can be used for a screening program due to its ability to generate results from a larger number of test compounds than a human operator could generate using the apparatus in a manual fashion.

15   **Quantitation of the influence**

The recording of the variation or result with respect to light emitted from the luminophore is performed by recording the spatially distributed light as one or more digital images, and the processing of the recorded variation to reduce it to one or more numbers representative of the degree of redistribution comprises a digital image processing procedure or combination
20   of digital image processing procedures. The quantitative information which is indicative of the degree of the cellular response to the influence or the result of the influence on the intracellular pathway is extracted from the recording or recordings according to a predetermined calibration based on responses or results, recorded in the same manner, to known degrees of a relevant specific influence. This calibration procedure is developed according to principles
25   described below (Developing an Image-based Assay Technique). Specific descriptions of the procedures for particular assays are given in the examples.

While the stepwise procedure necessary to reduce the image or images to the value representative of the is particular to each assay, the individual steps are generally well-known methods of image processing. Some examples of the individual steps are point operations
30   such as subtraction, ratioing, and thresholding, digital filtering methods such as smoothing, sharpening, and edge detection, spatial frequency methods such as Fourier filtering, image cross-correlation and image autocorrelation, object finding and classification (blob analysis),

10

and colour space manipulations for visualisation. In addition to the algorithmic procedures, heuristic methods such as neural networks may also be used.

Nucleic acid constructs

5   The nucleic acid constructs used in the present invention encode in their nucleic acid sequences fusion polypeptides comprising a biologically active polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and a GFP, preferably an F64L mutant of GFP, N- or C-terminally fused, optionally via a peptide linker, to the biologically active polypeptide or part thereof.

10   In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein kinase or a phosphatase.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a transcription factor or a part thereof which changes cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct
15   is a protein, or a part thereof, which is associated with the cytoskeletal network and which changes cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein kinase or a part thereof which changes cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct
20   is a serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a tyrosine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

25   In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a phospholipid-dependent serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cAMP-dependent protein kinase or a part thereof capable of changing cellular localisati-
30   on upon activation. In a preferred embodiment the biologically active polypeptide encoded by the nucleic acid construct is a PKAc-F64L-S65T-GFP fusion.

11

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cGMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct

5   is a calmodulin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a mitogen-activated serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation. In preferred embodiments the biologically active poly-

10   peptide encoded by the nucleic acid constructs are an ERK1-F64L-S65T-GFP fusion or an EGFP-ERK1 fusion.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cyclin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

15   In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein phosphatase or a part thereof capable of changing cellular localisation upon activation.

In one preferred embodiment of the invention the nucleic acid constructs may be DNA constructs.

20   In one embodiment the biologically active polypeptide encoded by the nucleic acid construct In one embodiment the gene encoding GFP in the nucleic acid construct is derived from Aequorea victoria. In a preferred embodiment the gene encoding GFP in the nucleic acid construct is EGFP or a GFP variant selected from F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP.

25   In preferred embodiments of the invention the DNA constructs which can be identified by any of the DNA sequences shown in SEQ ID NO: 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142 or are variants of these sequences capable of encoding the same fusion polypeptide or a fusion polypeptide which is biologically equivalent thereto,

30   e.g. an isoform, or a splice variant or a homologue from another species.

12

Screening program

The present invention describes a method that may be used to establish a screening program for the identification of biologically active substances that directly or indirectly affects intracellular signalling pathways and because of this property are potentially useful as me-
5   dicaments. Based on measurements in living cells of the redistribution of spatially resolved luminescence from luminophores which undergo a change in distribution upon activation or deactivation of an intracellular signalling pathway the result of the individual measurement of each substance being screened indicates its potential biological activity.

In one embodiment of the invention the screening program is used for the identification of a
10   biologically toxic substance as defined herein that exerts its toxic effect by interfering with an intracellular signalling pathway. Based on measurements in living cells of the redistribution of spatially resolved luminescence from luminophores which undergo a change in distribution upon activation or deactivation of an intracellular signalling pathway the result of the individual measurement of each substance being screened indicates its potential biologically toxic
15   activity. In one embodiment of a screening program a compound that modulates a component of an intracellular pathway as defined herein, can be found and the therapeutic amount of the compound estimated by a method according to the method of the invention. In a preferred embodiment the present invention leads to the discovery of a new way of treating a condition or disease related to the intracellular function of a biologically active polypeptide
20   comprising administration to a patient suffering from said condition or disease of an effective amount of a compound which has been discovered by any method according to the invention. In another preferred embodiment of the invention a method is established for identification of a new drug target or several new drug targets among the group of biologically active polypeptides which are components of intracellular signalling pathways.

25   In another embodiment of the invention an individual treatment regimen is established for the selective treatment of a selected patient suffering from an ailment where the available medicaments used for treatment of the ailment are tested on a relevant primary cell or cells obtained from said patient from one or several tissues, using a method comprising transfecting the cell or cells with at least one DNA sequence encoding a fluorescent probe ac-
30   cording to the invention, transferring the transfected cell or cells back the said patient, or culturing the cell or cells under conditions permitting the expression of said probes and exposing it to an array of the available medicaments, then comparing changes in fluorescence patterns or redistribution patterns of the fluorescent probes in the intact living cell or cells to

detect the cellular response to the specific medicaments (obtaining a cellular action profile), then selecting one or more medicament or medicaments based on the desired activity and acceptable level of side effects and administering an effective amount of these medicaments to the selected patient.

5

Back-tracking of a signal transduction pathway

The present invention describes a method that may be used to establish a screening program for back-tracking signal transduction pathways as defined herein. In one embodiment the screening program is used to establish more precisely at which level one or several

10   compounds affect a specific signal transduction pathway by successively or in parallel testing the influence of the compound or compounds on the redistribution of spatially resolved luminescence from several of the luminophores which undergo a change in distribution upon activation or deactivation of the intracellular signalling pathway under study.

15   ## Construction and testing of probes

In general, a probe, i.e. a "GeneX"-GFP fusion or a GFP-"GeneX" fusion, is constructed using PCR with "GeneX"-specific primers followed by a cloning step to fuse "GeneX" in-frame with GFP. The fusion may contain a short vector derived sequence between "GeneX" and GFP (e.g. part of a multiple cloning site region in the plasmid) resulting in a peptide lin-

20   ker between "GeneX" and GFP in the resulting fusion protein.

Detailed stepwise procedure:

- Identifying the sequence of the gene. This is most readily done by searching a depository of genetic information, e.g. the GenBank Sequence Database, which is widely available and

25   routinely used by molecular biologists. In the specific examples below the GenBank Accession number of the gene in question is provided.

- Design of gene-specific primers. Inspection of the sequence of the gene allows design of gene-specific primers to be used in a PCR reaction. Typically, the top-strand primer en-

30   compasses the ATG start codon of the gene and the following ca. 20 nucleotides, while the bottom-strand primer encompasses the stop codon and the ca. 20 preceding nucleotides, if

SUBSTITUTE SHEET (RULE 26)

14

the gene is to be fused behind GFP, i.e. a GFP-"GeneX" fusion. If the gene is to be fused in front of GFP, i.e. a "GeneX"-GFP fusion, a stop codon must be avoided. Optionally, the full length sequence of GeneX may not be used in the fusion, but merely the part which localizes and redistributes like GeneX in response to a signal.

5

In addition to gene-specific sequences, the primers contain at least one recognition sequence for a restriction enzyme, to allow subsequent cloning of the PCR product. The sites are chosen so that they are unique in the PCR product and compatible with sites in the cloning vector. Furthermore, it may be necessary to include an exact number of nucleotides between

10   the restriction enzyme site and the gene-specific sequence in order to establish the correct reading frame of the fusion gene and/or a translation initiation consensus sequence. Lastly, the primers always contain a few nucleotides in front of the restriction enzyme site to allow efficient digestion with the enzyme.

15   -Identifying a source of the gene to be amplified. In order for a PCR reaction to produce a product with gene-specific primers, the gene-sequence must initially be present in the reaction, e.g. in the form of cDNA. Information in GenBank or the scientific literature will usually indicate in which tissue(s) the gene is expressed, and cDNA libraries from a great variety of tissues or cell types from various species are commercially available, e.g. from Clontech

20   (Palo Alto), Stratagene (La Jolla) and Invitrogen (San Diego). Many genes are also available in cloned form from The American Type Tissue Collection (Virginia).

- Optimizing the PCR reaction. Several factors are known to influence the efficiency and specificity of a PCR reaction, including the annealing temperature of the primers, the con-

25   centration of ions, notably Mg^{2+} and K^+, present in the reaction, as well as pH of the reaction. If the result of a PCR reaction is deemed unsatisfactory, it might be because the parameters mentioned above are not optimal. Various annealing temperatures should be tested, e.g. in a PCR machine with a built-in temperature gradient, available from e.g. Stratagene (La Jolla), and/or various buffer compositions should be tried, e.g. the OptiPrime buffer system from

30   Stratagene (La Jolla).

SUBSTITUTE SHEET (RULE 26)

- Cloning the PCR product. The vector into which the amplified gene product will be cloned and fused with GFP will already have been taken into consideration when the primers were designed. When choosing a vector, one should at least consider in which cell types the probe subsequently will be expressed, so that the promoter controlling expression of the probe

5   is compatible with the cells. Most expression vectors also contain one or more selective markers, e.g. conferring resistance to a drug, which is a useful feature when one wants to make stable transfectants. The selective marker should also be compatible with the cells to be used.

10   The actual cloning of the PCR product should present no difficulty as it typically will be a one-step cloning of a fragment digested with two different restriction enzymes into a vector digested with the same two enzymes. If the cloning proves to be problematic, it may be because the restriction enzymes did not work well with the PCR fragment. In this case one could add longer extensions to the end of the primers to overcome a possible difficulty of di-

15   gestion close to a fragment end, or one could introduce an intermediate cloning step not based on restriction enzyme digestion. Several companies offer systems for this approach, e.g. Invitrogen (San Diego) and Clontech (Palo Alto).

Once the gene has been cloned and, in the process, fused with the GFP gene, the resulting

20   product, usually a plasmid, should be carefully checked to make sure it is as expected. The most exact test would be to obtain the nucleotide sequence of the fusion-gene.

Testing the probe

Once a DNA construct for a probe has been generated, its functionality and usefulness may

25   be tested by subjecting it to the following tests:

- Transfecting it into cells capable of expressing the probe. The fluorescence of the cell is inspected soon after, typically the next day. At this point, two features of cellular fluorescence are noted: the intensity and the sub-cellular localization.

30

SUBSTITUTE SHEET (RULE 26)

16

The intensity should usually be at least as strong as that of unfused GFP in the cells. If it is not, the sequence or quality of the probe-DNA might be faulty, and should be carefully checked.

5   The sub-cellular localization is an indication of whether the probe is likely to perform well. If it localizes as expected for the gene in question, e.g. is excluded from the nucleus, it can immediately go on to a functional test. If the probe is not localized soon after the transfection procedure, it may be because of overexpression at this point in time, as the cell typically will have taken of very many copies of the plasmid, and localization will occur in time, e.g. within

10   a few weeks, as plasmid copy number and expression level decreases. If localization does not occur after prolonged time, it may be because the fusion to GFP has destroyed a localization function, e.g. masked a protein sequence essential for interaction with its normal cellular anchor-protein. In this case the opposite fusion might work, e.g. if GeneX-GFP does not work, GFP-GeneX might, as two different parts of GeneX will be affected by the proximity to

15   GFP. If this does not work, the proximity of GFP at either end might be a problem, and it could be attempted to increase the distance by incorporating a longer linker between GeneX and GFP in the DNA construct.

If there is no prior knowledge of localization, and no localization is observed, it may be because the probe should not be localized at this point, because such is the nature of the pro-

20   tein fused to GFP. It should then be subjected to a functional test.

In a functional test, the cells expressing the probe are treated with at least one compound known to perturb, usually by activating, the signalling pathway on which the probe is expected to report by redistributing itself within the cell. If the redistribution is as expected, e.g. if prior knowledge tell that it should translocate from location X to location Y, it has passed the

25   first critical test. In this case it can go on to further characterization and quantification of the response.

If it does not perform as expected, it may be because the cell lacks at least one component of the signalling pathway, e.g. a cell surface receptor, or there is species incompatibility, e.g. if the probe is modelled on sequence information of a human geneproduct, and the cell is of

30   hamster origin. In both instances one should identify other cell types for the testing process where these potential problems would not apply.

If there is no prior knowledge about the pattern of redistribution, the analysis of the redistribution will have to be done in greater depth to identify what the essential and indicative features are, and when this is clear, it can go on to further characterization and quantification of the response. If no feature of redistribution can be identified, the problem might be as menti-

5 oned above, and the probe should be retested under more optimal cellular conditions.

If the probe does not perform under optimal cellular conditions it's back to the drawing board.

Developing an image-based assay technique

The process of developing an image-based redistribution assay begins with either the un-

10 planned experimental observation that a redistribution phenomenon can be visualised, or the design of a probe specifically to follow a redistribution phenomenon already known to occur. In either event, the first and best exploratory technique is for a trained scientist or technician to observe the phenomenon. Even with the rapid advances in computing technology, the human eye-brain combination is still the most powerful pattern recognition system known,

15 and requires no advance knowledge of the system in order to detect potentially interesting and useful patterns in raw data. This is especially if those data are presented in the form of images, which are the natural "data type" for human visual processing. Because human visual processing operates most effectively in a relatively narrow frequency range, i.e., we cannot see either very fast or very slow changes in our visual field, it may be necessary to

20 record the data and play it back with either time dilation or time compression.

Some luminescence phenomena cannot be seen directly by the human eye. Examples include polarization and fluorescence lifetime. However, with suitable filters or detectors, these signals can be recorded as images or sequences of images and displayed to the human in the fashion just described. In this way, patterns can be detected and the same methods can

25 be applied.

Once the redistribition has been determined to be a reproducible phenomenon, one or more data sets are generated for the purpose of developing a procedure for extracting the quantitative information from the data. In parallel, the biological and optical conditions are determined which will give the best quality raw data for the assay. This can become an iterative pro-

30 cess; it may be necessary to develop a quantitative procedure in order to assess the effect on the assay of manipulating the assay conditions.

The data sets are examined by a person or persons with knowledge of the biological phe-
nomenon and skill in the application of image processing techniques. The goal of this exerci-
se is to determine or at least propose a method which will reduce the image or sequence of
images constituting the record of a "response" to a value corresponding to the degree of the

5   response. Using either interactive image processing software or an image processing tool-
box and a programming language, the method is encoded as a procedure or algorithm which
takes the image or images as input and generates the degree of response (in any units) as
its output. Some of the criteria for evaluating the validity of a particular procedure are:

- Does the degree of the response vary in a biologically significant fashion, i.e., does it
10   show the known or putative dependence on the concentration of the stimulating
        agent or condition?

- Is the degree of response reproducible, i.e., does the same concentration or level of
        stimulating agent or condition give the same response with an acceptable variance?

- Is the dynamic range of the response sufficient for the purpose of the assay? If not,
15   can a change in the procedure or one of its parameters improve the dynamic range?

- Does the procedure exhibit any clear "pathologies", i.e., does it give ridiculous values
        for the response if there are commonly occurring imperfections in the imaging pro-
        cess? Can these pathologies be eliminated, controlled, or accounted for?

- Can the procedure deal with the normal variation in the number and/or size of cells in
20   an image?

In some cases the method may be obvious; in others, a number of possible procedures may
suggest themselves. Even if one method appears clearly superior to others, optimisation of
parameters may be required. The various procedures are applied to the data set and the
25   criteria suggested above are determined, or the single procedure is applied repeatedly with
adjustment of the parameter or parameters until the most satisfactory combination of signal,
noise, range, etc. are arrived at. This is equivalent to the calibration of any type of single-
channel sensor.

The number of ways of extracting a single value from an image are extremely large, and
30   thus an intelligent approach must be taken to the initial step of reducing this number to a
small, finite number of possible procedures. This is not to say that the procedure arrived at is

necessarily the best procedure - but a global search for the best procedure is simply out of the question due to the sheer number of possibilities involved.

Image-based assays are no different than other assay techniques in that their usefulness is characterised by parameters such as the specificity for the desired component of the

5   sample, the dynamic range, the variance, the sensitivity, the concentration range over which the assay will work, and other such parameters. While it is not necessary to characterise e-ach and every one of these before using the assay, they represent the only way to compare one assay with another.

10   <u>Example: Developing a Quantitative assay for GLUT4 Translocation</u>

GLUT4 is a member of the class of glucose transporter molecules which are important in cellular glucose uptake. It is known to translocate to the plasma membrane under some conditions of stimulation of glucose uptake. The ability to visualize the glucose uptake re-sponse noninvasively, without actually measuring glucose uptake, would be a very useful

15   assay for anyone looking for, for example, treatments for type II diabetes.

A CHO cell line which stably expressed the human insulin receptor was used as the basis for a new cell line which stably expressed a fusion between GLUT4 and GFP. This cell line was expected to show translocation of GLUT4 to the plasma membrane as visualized by the movement of the GFP. The translocation could definitely be seen in the form of the appea-

20   rance of local increases in the fluorescence in regions of the plasma membrane which had a characteristic shape or pattern. This is shown in Figure 12.

These objects became known as "snircles", and the phenomenon of their appearance as "snircling". In order to quantitate their appearance, a method had to be found to isolate them as objects in the image field, and then enumerate them, measure their area, or determine

25   some parameter about them which correlated in a dose-dependent fashion with the concen-tration of insulin to which the cells had been exposed. In order to separate the snircles, a bi-narization procedure was applied in which one copy of the image smoothed with a relatively severe gaussian kernel (sigma = 2.5) was subtracted from another copy to which only a re-latively light gaussian smooth had been applied (sigma=0.5). The resultant image was re-

30   scaled to its min/max range, and an automatic threshold was applied to divide the image into two levels. The thresholded image contains a background of one value all found object with another value. The found objects were first filtered through a filter to remove objects far too

20

large and far too small to be snircles. The remaining objects, which represent snircles and other artifacts from the image with approximately the same size and intensity characteristics as snircles, are passed into a classification procedure which has been previously trained with many images of snircles to recognize snircles and exclude the other artifacts. The result of

5   this procedure is a binary image which shows only the found snircles to the degree to which the classification procedure can accurately identify them. The total area of the snircles is then summed and this value is the quantitative measure of the degree of snircling for that image.

10 **Definitions:**

In the present specification and claims, the term "an influence" covers any influence to which the cellular response comprises a redistribution. Thus, e.g., heating, cooling, high pressure, low pressure, humidifying, or drying are influences on the cellular response on which the resulting redistribution can be quantified, but as mentioned above, perhaps the most important

15 influences are the influences of contacting or incubating the cell or cells with substances which are known or suspected to exert and influence on the cellular response involving a redistribution contribution. In another embodiment of the invention the influence could be substances from a compound drug library.

20 In the present context, the term "green fluorescent protein" is intended to indicate a protein which, when expressed by a cell, emits fluorescence upon exposure to light of the correct excitation wavelength (cf. [(Chalfie *et al.*1994)]). In the following, GFP in which one or more amino acids have been substituted, inserted or deleted is most often termed "modified GFP". "GFP" as used herein includes wild-type GFP derived from the jelly fish *Aequorea victoria*

25 and modifications of GFP, such as the blue fluorescent variant of GFP disclosed by Heim et al. (1994). Proc.Natl.Acad.Sci. 91:12501, and other modifications that change the spectral properties of the GFP fluorescence, or modifications that exhibit increased fluorescence when expressed in cells at a temperature above about 30°C described in PCT/DK96/00051, published as WO 97/11094 on 27 March 1997 and hereby incorporated by reference, and

30 which comprises a fluorescent protein derived from *Aequorea* Green Fluorescent Protein (GFP) or any functional analogue thereof, wherein the amino acid in position 1 upstream from the chromophore has been mutated to provide an increase of fluorescence intensity when the

fluorescent protein of the invention is expressed in cells. Preferred GFP variants are F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP. An especially preferred variant of GFP for use in all the aspects of this invention is EGFP (DNA encoding EGFP which is a F64L-S65T variant with codons optimized for expression in mammalian cells is available from Clontech,

5   Palo Alto, plasmids containing the EGFP DNA sequence, cf. GenBank Acc. Nos. U55762, U55763).

The term "intracellular signalling pathway" and "signal transduction pathway" are intended to indicate the coordinated intracellular processes whereby a living cell transduce an external

10   or internal signal into cellular responses. Said signal transduction will involve an enzymatic reaction said enzymes include but are not limited to protein kinases, GTPases, ATPases, protein phosphatases, phospholipases. The cellular responses include but are not limited to gene transcription, secretion, proliferation, mechanical activity, metabolic activity, cell death.

15   The term "second messenger" is used to indicate a low molecular weight component involved in the early events of intracellular signal transduction pathways.

The term "luminophore" is used to indicate a chemical substance which has the property of emitting light either inherently or upon stimulation with chemical or physical means. This includes but is not limited to fluorescence, bioluminescence, phosphorescence, chemilumine-

20   scence.

The term "mechanically intact living cell" is used to indicate a cell which is considered living according to standard criteria for that particular type of cell such as maintenance of normal membrane potential, energy metabolism, proliferative capability, and has not experienced

25   any physically invasive treatment designed to introduce external substances into the cell such as microinjection.

The term "physiologically relevant" ,when applied to an experimentally determined redistribution of an intracellular component, as measured by a change in the luminescence properties

30   or distribution, is used to indicate that said redistribution can be explained in terms of the underlying biological phenomenon which gives rise to the redistribution.

Th terms "image processing" and "image analysis" are used to describe a large family of digital data analysis techniques or combination of such techniques which reduce ordered arrays of numbers (images) to quantitative information describing those ordered arrays of numbers. When said ordered arrays of numbers represent measured values from a physical

5   process, the quantitative information derived is therefore a measure of the physical process.

The term "fluorescent probe" is used to indicate a fluorescent fusion polypeptide comprising a GFP or any functional part thereof which is N- or C-terminally fused to a biologically active polypeptide as defined herein, optionally via a peptide linker consisting of one or more amino

10   acid residues, where the size of the linker peptide in itself is not critical as long as the desired functionality of the fluorescent probe is maintained. A fluorescent probe according to the invention is expressed in a cell and basically mimics the physiological behaviour of the biologically active polypeptide moiety of the fusion polypeptide.

15   The term "mammalian cell" is intended to indicate any living cell of mammalian origin. The cell may be an established cell line, many of which are available from The American Type Culture Collection (ATCC, Virginia, USA) or a primary cell with a limited life span derived from a mammalian tissue, including tissues derived from a transgenic animal, or a newly established immortal cell line derived from a mammalian tissue including transgenic tissues,

20   or a hybrid cell or cell line derived by fusing different celltypes of mammalian origin e.g. hybridoma cell lines. The cells may optionally express one or more non-native gene products, e.g. receptors, enzymes, enzyme substrates, prior to or in addition to the fluorescent probe. Preferred cell lines include but are not limited to those of fibroblast origin, e.g. BHK, CHO, BALB, or of endothelial origin, e.g. HUVEC, BAE (bovine artery endothelial), CPAE (cow

25   pulmonary artery endothelial) or of pancreatic origin, e.g. RIN, INS-1, MIN6, bTC3, aTC6, bTC6, HIT, or of hematopoietic origin, e.g. adipocyte origin, e.g. 3T3-L1, neuronal/neuroendocrine origin, e.g. AtT20, PC12, GH3, muscle origin, e.g. SKMC, A10, C2C12, renal origin, e.g. HEK 293, LLC-PK1.

The term "hybrid polypeptide" is intended to indicate a polypeptide which is a fusion of at le-

30   ast a portion of each of two proteins, in this case at least a portion of the green fluorescent protein, and at least a portion of a catalytic and/or regulatory domain of a protein kinase. Furthermore a hybrid polypeptide is intended to indicate a fusion polypeptide comprising a

GFP or at least a portion of the green fluorescent protein that contains a functional fluorop-
hore, and at least a portion of a biologically active polypeptide as defined herein provided
that said fusion is not the PKCα-GFP, PKCγ-GFP, and PKCε-GFP disclosed by Schmidt et
al.and Sakai et al., respectively. Thus, GFP may be N- or C-terminally tagged to a biologi-
5   cally active polypeptide, optionally via a linker portion or linker peptide consisting of a sequ-
ence of one or more amino acids. The hybrid polypeptide or fusion polypeptide may act as a
fluorescent probe in intact living cells carrying a DNA sequence encoding the hybrid poly-
peptide under conditions permitting expression of said hybrid polypeptide.

10   The term "kinase" is intended to indicate an enzyme that is capable of phosphorylating a
cellular component.

The term "protein kinase" is intended to indicate an enzyme that is capable of phosphoryla-
ting serine and/or threonine and/or tyrosine in peptides and/or proteins.

15   The term "phosphatase" is intended to indicate an enzyme that is capable of dephosphoryla-
ting phosphoserine and/or phosphothreonine and/or phosphotyrosine in peptides and/or
proteins.

In the present context, the term "biologically active polypeptide" is intended to indicate a po-
20   lypeptide affecting intracellular processes upon activation, such as an enzyme which is acti-
ve in intracellular processes or a portion thereof comprising a desired amino acid sequence
which has a biological function or exerts a biological effect in a cellular system. In the poly-
peptide one or several aminoacids may have been deleted, inserted or replaced to alter its
biological function, e.g. by rendering a catalytic site inactive. Preferably, the biologically acti-
25   ve polypeptide is selected from the group consisting of proteins taking part in an intracellular
signalling pathway, such as enzymes involved in the intracellular phosphorylation and dep-
hosphorylation processes including kinases, protein kinases and phosphorylases as defined
herein, but also proteins making up the cytoskeleton play important roles in intracellular sig-
nal transduction and are therefore included in the meaning of "biologically active polypeptide"
30   herein. More preferably, the biologically active polypeptide is a protein which according to its
state as activated or non-activated changes localisation within the cell, preferably as an in-

24

termediary component in a signal transduction pathway. Included in this preferred group of biologically active polypeptides are cAMP dependent protein kinase A.

The term "a substance having biological activity" is intended to indicate any sample which
5   has a biological function or exerts a biological effect in a cellular system. The sample may be a sample of a biological material such as a sample of a body fluid including blood, plasma, saliva, milk, urine, or a microbial or plant extract, an environmental sample containing pollutants including heavy metals or toxins, or it may be a sample containing a compound or mixture of compounds prepared by organic synthesis or genetic techniques.

10

The phrase "any change in fluorescence" means any change in absorption properties, such as wavelength and intensity, or any change in spectral properties of the emitted light, such as a change of wavelength, fluorescence lifetime, intensity or polarisation, or any change in the intracellular localisation of the fluorophore. It may thus be localised to a specific cellular
15   component (e.g. organelle, membrane, cytoskeleton, molecular structure) or it may be evenly distributed throughout the cell or parts of the cell.

The phrase "back-tracking of a signal transduction pathway" is intended to indicate.

The term "organism" as used herein indicates any unicellular or multicellular organism preferably originating from the animal kingdom including protozoans, but also organisms that are
20   members of the plant kingdoms, such as algae, fungi, bryophytes, and vascular plants are included in this definition.

The term "nucleic acid" is intended to indicate any type of poly- or oligonucleic acid sequence, such as a DNA sequence, a cDNA sequence, or an RNA sequence.

25

The term "biologically equivalent" as it relates to proteins is intended to mean that a first protein is equivalent to a second protein if the cellular functions of the two proteins may substitute for each other, e.g. if the two proteins are closely related isoforms encoded by different genes, if they are splicing variants, or allelic variants derived from the same gene, if
30   they perform identical cellular functions in different cell types, or in different species. The term "biologically equivalent" as it relates to DNA is intended to mean that a first DNA sequ-

ence encoding a polypeptide is equivalent to a second DNA sequence encoding a polypepti-
de if the functional proteins encoded by the two genes are biologically equivalent.

The phrase "back-tracking of a signal transduction pathway" is intended to indicate a process
5   for defining more precisely at what level a signal transduction pathway is affected, either by
the influence of chemical compounds or a disease state in an organism. Consider a specific
signal transduction pathway represented by the bioactive polypeptides A - B - C - D, with
signal transduction from A towards D. When investigating all components of this signal
transduction pathway compounds or disease states that influence the activity or redistribu-
10   tion of only D can be considered to act on C or downstream of C whereas compounds or
disease states that influence the activity or redistribution of C and D, but not of A and B can
be considered to act downstream of B.

The term "fixed cells" is used to mean cells treated with a cytological fixative such as glu-
15   taraldehyde or formaldehyde, treatments which serve to chemically cross-link and stabilize
soluble and insoluble proteins within the structure of the cell. Once in this state, such pro-
teins cannot be lost from the structure of the now-dead cell.

20

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. CHO cells expressing the PKAc-F64L-S65T-GFP hybrid protein have been treated
in HAM's F12 medium with 50 mM forskolin at 37°C. The images of the GFP fluorescence in
25   these cells have been taken at different time intervals after treatment, which were: a) 40 se-
conds b) 60 seconds c) 70 seconds d) 80 seconds. The fluorescence changes from a
punctate to a more even distribution within the (non-nuclear) cytoplasm.

Figure 2. Time-lapse analysis of forskolin induced PKAc-F64L-S65T-GFP redistribution. CHO cells, expressing the PKAc-F64L-S65T-GFP fusion protein were analysed by time-lapse fluorescence microscopy. Fluorescence micrographs were acquired at regular intervals from 2 min before to 8 min after the addition of agonist. The cells were challenged with 1 mM

5   forskolin immediately after the upper left image was acquired (t=0). Frames were collected at the following times: i) 0, ii) 1, iii) 2, iv) 3, v) 4 and vi) 5 minutes. Scale bar 10 mm.

Figure 3. Time-lapse analyses of PKAc-F64L-S65T-GFP redistribution in response to various

10   agonists. The effects of 1 mM forskolin (A), 50 mM forskolin (B), 1mM dbcAMP (C) and 100 mM IBMX (D) (additions indicated by open arrows) on the localisation of the PKAc-F64L-S65T-GFP fusion protein were analysed by time-lapse fluorescence microscopy of CHO/PKAc-F64L-S65T-GFP cells. The effect of addition of 10 mM forskolin (open arrow), followed shortly by repeated washing with buffer (solid arrow), on the localisation of the

15   PKAc-F64L-S65T-GFP fusion protein was analysed in the same cells (E). In a parallel experiment, the effect of adding 10 mM forskolin and 100 mM IBMX (open arrow) followed by repeated washing with buffer containing 100 mM IBMX (solid arrow) was analysed (F). Removing forskolin caused PKAc-F64L-S65T-GFP fusion protein to return to the cytoplasmic aggregates while this is prevented by the continued presence of IBMX (F). The effect of 100

20   nM glucagon (Fig 3G, open arrow) on the localisation of the PKAc-F64L-S65T-GFP fusion protein is also shown for BHK/GR, PKAc-F64L-S65T-GFP cells. The effect of 10 mM norepinephrine (H), solid arrow, on the localisation of the PKAc-F64L-S65T-GFP fusion protein was analysed similarly, in transiently transfected CHO, PKAc-F64L-S65T-GFP cells, pretreated with 10 mM forskolin, open arrow, to increase [cAMP]$_i$. N.B. in Fig 3H the x-axis counts

25   the image numbers, with 12 seconds between images. The raw data of each experiment consisted of 60 fluorescence micrographs acquired at regular intervals including several images acquired before the addition of buffer or agonist. The charts (A-G) each show a quantification of the response seen through all the 60 images, performed as described in analysis method 2. The change in total area of the highly fluorescent aggregates, relative to

30   the initial area of fluorescent aggregates is plotted as the ordinate in all graphs in Figure 3, versus time for each experiment. Scale bar 10 mm.

27

Figure 4. Dose response curve (two experiments) for forskolin-induced redistribution of the PKAc-F64L-S65T-GFP fusion.

5

Figure 5. Time from initiation of a response to half maximal ($t_{1/2max}$) and maximal (t_{max}) PKAc-F64L-S65T-GFP redistribution. The data was extracted from curves such as that shown in "Figure 2." All $t_{1/2max}$ and t_{max} values are given as mean±SD and are based on a total of 26-30 cells from 2-3 independent experiments for each forskolin concentration. Since the observed 10   redistribution is sustained over time, the t_{max} values were taken as the earliest time point at which complete redistribution is reached. Note that the values do not relate to the degree of redistribution.

15   Figure 6. Parallel dose response analyses of forskolin induced cAMP elevation and PKAc-F64L-S65T-GFP redistribution. The effects of buffer or 5 increasing concentrations of forskolin on the localisation of the PKAc-F64L-S65T-GFP fusion protein in CHO/PKAc-F64L-S65T-GFP cells, grown in a 96 well plate, were analysed as described above. Computing the ratio of the SD's of fluorescence micrographs taken of the same field of cells, prior to and 30 min 20   after the addition of forskolin, gave a reproducible measure of PKAc-F64L-S65T-GFP redistribution. The graph shows the individual 48 measurements and a trace of their mean±s.e.m at each forskolin concentration. For comparison, the effects of buffer or 8 increasing concentrations of forskolin on [cAMP]$_i$ was analysed by a scintillation proximity assay of cells grown under the same conditions. The graph shows a trace of the mean ± s.e.m of 4 25   experiments expressed in arbitrary units.

Figure 7. BHK cells stably transfected with the human muscarinic (hM1) receptor and the PKCa-F64L-S65T-GFP fusion. Carbachol (100 mM added at 1.0 second) induced a transient redistribution of PKCa-F64L-S65T-GFP from the cytoplasm to the plasma membrane. Ima-30   ges were taken at the following times: a) 1 second before carbachol addition, b) 8.8 seconds after addition and c) 52.8 seconds after addition.

Figure 8. BHK cells stably transfected with the hM1 receptor and PKCa-F64L-S65T-GFP fusion were treated with carbachol (1 mM, 10 mM, 100 mM). In single cells intracellular $[Ca^{2+}]$ was monitored simultaneously with the redistribution of PKCa-F64L-S65T-GFP. Da-

5   shed line indicates the addition times of carbachol. The top panel shows changes in the intracellular Ca^{2+} concentration of individual cells with time for each treatment. The middle panel shows changes in the average cytoplasmic GFP fluorescence for individual cells against time for each treatment. The bottom panel shows changes in the fluorescence of the periphery of single cells, within regions that specifically include the circumferential edge of a cell

10   as seen in normal projection, the regions which offers best chance to monitor changes in the fluorescence intensity of the plasma membrane.

Figure 9. a) The hERK1-F64L-S65T-GFP fusion expressed in HEK293 cells treated with 100 mM of the MEK1 inhibitor PD98059 in HAM F-12 (without serum) for 30 minutes at 37 °C.

15   The nuclei empty of fluorescence during this treatment.

b) The same cells as in (a) following treatment with 10 % foetal calf serum for 15 minutes at 37 °C.

c) Time profiles for the redistribution of GFP fluorescence in HEK293 cells following treatment with various concentrations of EGF in Hepes buffer (HAM F-12 replaced with Hepes

20   buffer directly before the experiment). Redistribution of fluorescence is expressed as the change in the ratio value between areas in nucleus and cytoplasm of single cells. Each time profile is the mean for the changes seen in six single cells.

d) Bar chart for the end-point measurements, 600 seconds after start of EGF treatments, of fluorescence change (nucleus:cytoplasm) following various concentrations of EGF.

25

Figure 10.

a) The SMAD2-EGFP fusion expressed in HEK293 cells starved of serum overnight in HAM F-12. HAM F-12 was then replaced with Hepes buffer pH 7.2 immediately before the experiment. Scale bar is 10 mm.

30   b) HEK 293 cells expressing the SMAD2-EGFP fusion were treated with various concentration of TGF-beta as indicated, and the redistribution of fluorescence monitored against time.

The time profile plots represent increases in fluorescence within the nucleus, normalised to starting values in each cell measured. Each trace is the time profile for a single cell nucleus.

c) A bar chart representing the end-point change in fluorescence within nuclei (after 850 seconds of treatment) for different concentrations of TGF-beta. Each bar is the value for a single nucleus in each treatment.

Figure 11. The VASP-F64L-S65T-GFP fusion in CHO cells stably transfected with the human insulin receptor. The cells were starved for two hours in HAM F-12 without serum, then treated with 10% foetal calf serum. The image shows the resulting redistribution of fluorescence after 15 minutes of treatment. GFP fluorescence becomes localised in structures identified as focal adhesions along the length of actin stress fibres.

Figure 12. Time lapse recording GLUT4-GFP redistribution in CHO-HIR cells. Time indicates minutes after the addition of 100 nM insulin.

30

EXAMPLE 1

5   Construction, testing and implementation of an assay for cAMP based on PKA activation in
     real time within living cells.

     Useful for monitoring the activity of signalling pathways which lead to altered concentrations
     of cAMP, e.g. activation of G-protein coupled receptors which couple to G-proteins of the G_s
     or G_i class.

10

     The catalytic subunit of the murine cAMP dependent protein kinase (PKAc)was fused C-
     terminally to a F64L-S65T derivative of GFP. The resulting fusion (PKAc-F64L-S65T-GFP)
     was used for monitoring *in vivo* the translocation and thereby the activation of PKA.

     Construction of the PKAc-F64L-S65T-GFP fusion:

15   Convenient restriction endonuclease sites were introduced into the cDNAs encoding murine
     PKAc (Gen Bank Accession number: M12303) and F64L-S65T-GFP (sequence disclosed in
     WO 97/11094) by polymerase chain reaction (PCR). The PCR reactions were performed ac-
     cording to standard protocols with the following primers:

     5'PKAc: TTggACACAAgCTTTggACACCCTCAggATATgggCAACgCCgCCgCCgCCAAg
20   (SEQ ID NO:3),

     3'PKAc: gTCATCTTCTCgAgTCTTTCAggCgCgCCCAAACTCAgTAAACTCCTTgCCACAC
     (SEQ ID NO:4) ,

     5'GFP: TTggACACAAgCTTTggACACggCgCgCCATgAgTAAAggAgAAgAACTTTTC (SEQ ID
     NO:1),

25   3'GFP: gTCATCTTCTCgAgTCTTACTCCTgAggTTTgTATAgTTCATCCATgCCATgT (SEQ ID
     NO:2).

SUBSTITUTE SHEET (RULE 26)

The PKAc amplification product was then digested with HindIII+AscI and the F64L-S65T-GFP product with AscI+XhoI. The two digested PCR products were subsequently ligated with a HindIII+XhoI digested plasmid (pZeoSV® mammalian expression vector, Invitrogen, San Diego, CA, USA). The resulting fusion construct (SEQ ID NO:68 & 69) was under con-
5   trol of the SV40 promoter.

Transfection and cell culture conditions.

Chinese hamster ovary cells (CHO), were transfected with the plasmid containing the PKAc-F64L-S65T-GFP fusion using the calcium phosphate precipitate method in HEPES-buffered saline (Sambrook et al., 1989). Stable transfectants were selected using 1000 mg Zeocin/ml
10   (Invitrogen) in the growth medium (DMEM with 1000 mg glucose/l, 10 % fetal bovine serum (FBS), 100 mg penicillin-streptomycin mixture ml^{-1}, 2 mM L-glutamine purchased from Life Technologies Inc., Gaithersburg, MD, USA). Untransfected CHO cells were used as the control. To assess the effect of glucagon on fusion protein translocation, the PKAc-F64L-S65T-GFP fusion was stably expressed in baby hamster kidney cells overexpressing the
15   human glucagon receptor (BHK/GR cells) Untransfected BHK/GR cells were used as the control. Expression of GR was maintained with 500 mg G418/ml (Neo marker) andPKAc-F64L-S65T-GFP was maintained with 500 mg Zeocin/ml (Sh ble marker). CHO cells were also simultaneously co-transfected with vectors containing the PKAc-F64L-S65T-GFP fusion and the human a2a adrenoceptor (hARa2a).

20   For fluorescence microscopy, cells were allowed to adhere to Lab-Tek chambered cover-glasses (Nalge Nunc Int., Naperville, IL, USA) for at least 24 hours and cultured to about 80% confluence. Prior to experiments, the cells were cultured over night without selection pressure in HAM F-12 medium with glutamax (Life Technologies), 100 mg penicillin-streptomycin mixture ml^{-1} and 0.3 % FBS. This medium has low autofluorescence enabling
25   fluorescence microscopy of cells straight from the incubator.

Monitoring activity of PKA activity in real time:

Image aquisition of live cells were gathered using a Zeiss Axiovert 135M fluorescence mi-croscope fitted with a Fluar 40X, NA: 1.3 oil immersion objective and coupled to a Photomet-
30   rics CH250 charged coupled device (CCD) camera. The cells were illuminated with a 100 W HBO arc lamp. In the light path was a 470±20 nm excitation filter, a 510 nm dichroic mirror

32

and a 515±15 nm emission filter for minimal image background. The cells were kept and monitored to be at 37°C with a custom built stage heater.

Images were processed and analyzed in the following manner:.

Method 1: Stepwise procedure for quantitation of translocation of PKA:

5   1. The image was corrected for dark current by performing a pixel-by-pixel subtraction of a dark image (an image taken under the same conditions as the actual image, except the camera shutter is not allowed to open).

2. The image was corrected for non-uniformity of the illumination by performing a pixel-by-pixel ratio with a flat field correction image (an image taken under the same conditions as the actual image of a uniformly fluorescent specimen).

10

3. The image histogram, i.e., the frequency of occurrence of each intensity value in the image, was calculated.

4. A smoothed, second derivative of the histogram was calculated and the second zero is determined. This zero corresponds to the inflection point of the histogram on the high side of the main peak representing the bulk of the image pixel values.

15

5. The value determined in step 4 was subtracted from the image. All negative values were discarded.

6. The variance (square of the standard deviation) of the remaining pixel values was determined. This value represents the "response" for that image.

20   7. Scintillation proximity assay (SPA) for independent quantitation of cAMP:

Method 2: Alternative method for quantitation of PKA redistribution:

5   1. The fluorescent aggregates are segmented from each image using an automatically found threshold based on the maximisation of the information measure between the object and background. The *a priori* entropy of the image histogram is used as the information measure.

2. The area of each image occupied by the aggregates is calculated by counting pixels in the segmented areas.

10   3. The value obtained in step 2 for each image in a series, or treatment pair, is normalised to the value found for the first (unstimulated) image collected. A value of zero (0) indicates no redistribution of fluorescence from the starting condition. A value of one (1) by this method equals full redistribution.

15   Cells were cultured in HAM F-12 medium as described above, but in 96-well plates. The medium was exchanged with Ca^{2+}-HEPES buffer including 100 mM IBMX and the cells were stimulated with different concentrations of forskolin for 10 min. Reactions were stopped with addition of NaOH to 0.14 M and the amount of cAMP produced was measured with the cAMP-SPA kit, RPA538 (Amersham) as described by the manufacturer.

20

Manipulating intracellular levels of cAMP to test the PKAc-F64L-S65T-GFP fusion.

The following compounds were used to vary cAMP levels: Forskolin, an activator of adenylate cyclase; dbcAMP, a membrane permeable cAMP analog which is not degraded by phosphodiesterase; IBMX, an inhibitor of phosphodiesterase.

25   CHO cells stably expressing the PKAc-F64L-S65T-GFP, showed a dramatic translocation of the fusion protein from a punctate distribution to an even distribution throughout the cytoplasm following stimulation with 1 mM forskolin (n=3), 10 mM forskolin (n=4) and 50 mM forskolin (n=4) (Fig 1), or dbcAMP at 1mM (n=6).

Fig. 2 shows the progression of response in time following treatment with 1 mM forskolin.

34

Fig. 3 gives a comparison of the average temporal profiles of fusion protein redistribution and a measure of the extent of each response to the three forskolin concentrations (Fig. 3A, E, B), and to 1 mM dbcAMP (fig 3C) which caused a similar but slower response, and to addition of 100 mM IBMX (n=4, Fig. 3D) which also caused a slow response, even in the absence of adenylate cyclase stimulation. Addition of buffer (n=2) had no effect (data not shown).

As a control for the behavior of the fusion protein, F64L-S65T-GFP alone was expressed in CHO cells and these were also given 50 mM forskolin (n=5); the uniform diffuse distribution characteristic of GFP in these cells was unaffected by such treatment (data not shown).

The forskolin induced translocation of PKAc-F64L-S65T-GFP showed a dose-response relationship (Fig 4 and 6), see quantitative procedures above.

Reversibility of PKAc-F64L-S65T-GFP translocation.

The release of the PKAc probe from its cytoplasmic anchoring hotspots was reversible. Washing the cells repeatedly (5-8 times) with buffer after 10µM forskolin treatment completely restored the punctate pattern within 2-5 min (n=2, Fig. 3E). In fact the fusion protein returned to a pattern of fluorescent cytoplasmic aggregates virtually indistinguishable from that observed before forskolin stimulation.

To test whether the return of fusion protein to the cytoplasmic aggregates reflected a decreased [cAMP]$_i$, cells were treated with a combination of 10 mM forskolin and 100 mM IBMX (n=2) then washed repeatedly (5-8 times) with buffer containing 100 mM IBMX (Fig. 3F). In these experiments, the fusion protein did not return to its prestimulatory localization after removal of forskolin.

Testing the PKA-F64L-S65T-GFP probe with physiologically relevant agents.

To test the probe's response to receptor activation of adenylate cyclase, BHK cells stably transfected with the glucagon receptor and the PKA-F64L-S65T-GFP probe were exposed to glucagon stimulation. The glucagon receptor is coupled to a G$_s$ protein which activates adenylate cyclase, thereby increasing the cAMP level. In these cells, addition of 100 nM glucagon (n=2) caused the release of the PKA-F64L-S65T-GFP probe from the cytoplasmic aggregates and a resulting translocation of the fusion protein to a more even cytoplasmic

SUBSTITUTE SHEET (RULE 26)

distribution within 2-3 min (Fig. 3G). Similar but less pronounced effects were seen at lower glucagon concentrations (n=2, data not shown). Addition of buffer (n=2) had no effect over time (data not shown).

Transiently transfected CHO cells expressing hARa2a and the PKA-F64L-S65T-GFP probe
5   were treated with 10 mM forskolin for 7.5 minutes, then, in the continued presence of forskolin, exposed to 10 mM norepinephrine to stimulate the exogenous adrenoreceptors, which couple to a G_i protein, which inhibit adenylate cyclase. This treatment led to reappearance of fluorescence in the cytoplasmic aggregates indicative of a decrease in $[cAMP]_i$ (Fig. 3H).

10

Fusion protein translocation correlated with $[cAMP]_i$

As described above, the time it took for a response to come to completion was dependent on the forskolin dose (Fig. 5) In addition the degree of responses was also dose dependent. To test the PKA-F64L-S65T-GFP fusion protein translocation in a semi high through-put sy-
15   stem, CHO cells stably transfected with the PKA-F64L-S65T-GFP fusion was stimulated with buffer and 5 increasing doses of forskolin (n=8). Using the image analysis algorithm described above (Method 1), a dose response relationship was observed in the range from 0.01-50 mM forskolin (Fig. 6). A half maximal stimulation was observed at about 2 mM forskolin. In parallel, cells were stimulated with buffer and 8 increasing concentrations of for-
20   skolin (n=4) in the range 0.01-50 mM. The amount of cAMP produced was measured in an SPA assay. A steep increase was observed between 1 and 5 mM forskolin coincident with the steepest part of the curve for fusion protein translocation (also Fig. 6)

25   EXAMPLE 2

Quantitation of redistribution in real-time within living cells.

Probe for detection of PKC activity in real time within living cells:

Construction of PKC-GFP fusion:

36

The probe was constructed by ligating two restriction enzyme treated polymerase chain re-
action (PCR) amplification products of the cDNA for murine PKCα (GenBank Accession
number: M25811) and F64L-S65T-GFP (sequence disclosed in WO 97/11094) respectively.
Taq® polymerase and the following oligonucleotide primers were used for PCR;

5   5'mPKCa: TTggACACAAgCTTTggACACCCTCAggATATggCTgACgTTTACCCggCCAACg
     (SEQ ID NO:5),

     3'mPKCa: gTCATCTTCTCgAgTCTTTCAggCgCgCCCTACTgCACTTTgCAAgATTgggTgC
     (SEQ ID NO:6),

     5'F64L-S65T-GFP: TTggACACAAgCTTTggACACggCgCgCCATgAgTAAAggAgAAgAACTT-
10   TTC (SEQ ID NO:1),

     3'F64L-S65T-GFP: gTCATCTTCTCgAgTCTTACTCCTgAggTTTgTATAgTTCATCCATgC-
     CATgT (SEQ ID NO:2).

     The hybrid DNA strand was inserted into the pZeoSV® mammalian expression vector as a
     HindIII-XhoI casette as described in example 1.

15   Cell Culture:

     BHK cells expressing the human M1 receptor under the control of the inducible metal-
     lothionine promoter and maintained with the dihydrofolate reductase marker were trans-
     fected with the PKCα-F64L-S65T-GFP probe using the calcium phosphate precipitate
     method in HEPES buffered saline (HBS [pH 7.10]). Stable transfectants were selected using
20   1000 µg Zeocin®/ml in the growth medium (DMEM with 1000 mg glucose/l, 10 % foetal bo-
     vine serum (FBS), 100 mg penicillin-streptomycin mixture ml-1, 2 mM l-glutamine). The hM1
     receptor and PKCα-F64L-S65T-GFP fusion protein were maintained with 500 nM
     methotrexate and 500 µg Zeocin®/ml respectively. 24 hours prior to any experiment, the
     cells were transferred to HAM F-12 medium with glutamax, 100 µg penicillin-streptomycin
25   mixture ml⁻¹ and 0.3 % FBS. This medium relieves selection pressure, gives a low induction
     of signal transduction pathways and has a low autofluorescence at the relevant wavelength
     enabling fluorescence microscopy of cells straight from the incubator.

     Monitoring the PKC activity in real time:

     Digital images of live cells were gathered using a Zeiss Axiovert 135M fluorescence micro-
30   scope fitted with a 40X, NA: 1.3 oil immersion objective and coupled to a Photometrics

CH250 charged coupled device (CCD) camera. The cells were illuminated with a 100 W arc lamp. In the light path was a 470±20 nm excitation filter, a 510 nm dichroic mirror and a 515±15 nm emission filter for minimal image background. The cells were kept and monitored to be at 37°C with a custom built stage heater.

5   Images were analyzed using the IPLab software package for Macintosh.

Upon stimulation of the M1-BHK cells, stably expressing the PKCα-F64L-S65T-GFP fusion, with carbachol we observed a dose-dependent transient translocation from the cytoplasm to the plasma membrane (Fig. 7a,b,c). Simultaneous measurement of the cytosolic free calcium concentration shows that the carbachol-induced calcium mobilisation precedes the

10   translocation (Fig. 8).

Stepwise procedure for quantitation of translocation of PKC:

1.   The image was corrected for dark current by performing a pixel-by-pixel subtraction of a dark image (an image taken under the same conditions as the actual image, except the camera shutter is not allowed to open).

15   2.   The image was corrected for non-uniformity of the illumination by performing a pixel-by-pixel ratio with a flat field correction image (an image taken under the same conditions as the actual image of a uniformly fluorescent specimen).

3.   A copy of the image was made in which the edges are identified. The edges in the image are found by a standard edge-detection procedure – convolving the image with a kernel

20   which removes any large-scale unchanging components (i.e., background) and accentuates any small-scale changes (i.e., sharp edges). This image was then converted to a binary image by threshholding. Objects in the binary image which are too small to represent the edges of cells were discarded. A dilation of the binary image was performed to close any gaps in the image edges. Any edge objects in the image which were in contact with the bor-

25   ders of the image are discarded. This binary image represents the edge mask.

4.   Another copy of image was made via the procedure in step 3. This copy was further processed to detect objects which enclose "holes" and setting all pixels inside the holes to the binary value of the edge, i.e., one. This image represents the whole cell mask.

5.   The original image was masked with the edge mask from step 3 and the sum total of all

30   pixel values is determined.

6. The original image was masked with the whole cell mask from step 4 and the sum total of all pixel values was determined.

7. The value from step 5 was divided by the value from step 6 to give the final result, the fraction of fluorescence intensity in the cells which was localized in the edges.

5

EXAMPLE 3

Probes for detection of mitogen activated protein kinase Erk1 redistribution.

Useful for monitoring signalling pathways involving MAPK, e.g. to identify compounds which
10 modulate the activity of the pathway in living cells.

Erk1, a serine/threonine protein kinase, is a component of a signalling pathway which is acti-
vated by e.g. many growth factors.

Probes for detection of ERK-1 activity in real time within living cells:

15 The extracellular signal regulated kinase (ERK-1, a mitogen activated protein kinase, MAPK)
is fused N- or C-terminally to a derivative of GFP. The resulting fusions expressed in differ-
ent mammalian cells are used for monitoring *in vivo* the nuclear translocation, and thereby
the activation, of ERK1 in response to stimuli that activate the MAPK pathway.

a) Construction of murine ERK1 - F64L-S65T-GFP fusion:

20 Convenient restriction endonuclease sites are introduced into the cDNAs encoding murine
ERK1 (GenBank Accession number: Z14249) and F64L-S65T-GFP (sequence disclosed in
WO 97/11094) by polymerase chain reaction (PCR). The PCR reactions are performed ac-
cording to standard protocols with the following primers:

5'ERK1: TTggACACAAgCTTTggACACCCTCAggATATggCggCggCggCggCggCTCCggggg-
25 gCgggg (SEQ ID NO:7),

3'ERK1: gTCATCTTCTCgAgTCTTTCAggCgCgCCCggggCCCTCTggCgCCCCTggCTgg
(SEQ ID NO:8),

5'F64L-S65T-GFP: TTggACACAAgCTTTggACACggCgCgCCATgAgTAAAggAgAAgAACTT-
TTC (SEQ ID NO:1)

5   3'F64L-S65T-GFP: gTCATCTTCTCgAgTCTTACTCCTgAggTTTgTATAgTTCATCCATgC-
CATgT (SEQ ID NO:2)

To generate the mERK1-F64L-S65T-GFP (SEQ ID NO:56 & 57) fusion the ERK1 amplifica-
tion product is digested with HindIII+AscI and the F64L-S65T-GFP product with AscI+XhoI.
To generate the F64L-S65T-GFP-mERK1 fusion the ERK1 amplification product is then di-
10   gested with HindIII+Bsu36I and the F64L-S65T-GFP product with Bsu36I+XhoI.The two
pairs of digested PCR products are subsequently ligated with a HindIII+XhoI digested plas-
mid (pZeoSV® mammalian expression vector, Invitrogen, San Diego, CA, USA). The resul-
ting fusion constructs are under control of the SV40 promoter.

15   b) The human Erk1 gene (GenBank Accession number: X60188) was amplified using PCR
according to standard protocols with primers Erk1-top (SEQ ID NO:9) and Erk1-
bottom/+stop (SEQ ID NO:10) . The PCR product was digested with restriction enzymes E-
coR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession
number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Erk1 fusion
20   (SEQ ID NO:38 &39) under the control of a CMV promoter.

The plasmid containing the EGFP-Erk1 fusion was transfected into HEK293 cells employing
the FUGENE transfection reagent (Boehringer Mannheim). Prior to experiments the cells
were grown to 80%-90% confluency 8 well chambers in DMEM with 10% FCS. The cells we-
25   re washed in plain HAM F-12 medium (without FCS), and then incubated for 30-60 minutes
in plain HAM F-12 (without FCS) with 100 micromolar PD98059, an inhibitor of MEK1, a ki-
nase which activates Erk1; this step effectively empties the nucleus of EGFP-Erk1. Just be-
fore starting the experiment, the HAM F-12 was replaced with Hepes buffer following a wash
with Hepes buffer. This removes the PD98059 inhibitor; if blocking of MEK1 is still wanted
30   (e.g. in control experiments), the inhibitor is included in the Hepes buffer.

The experimental setup of the microscope was as described in example 1.

40

60 images were collected with 10 seconds between each, and with the test compound added after image number 10.

Addition of EGF (1-100 nM) caused within minutes a redistribution of EGFP-Erk1 from the
5   cytoplasm into the nucleus (Fig. 9a,b).

The response was quantitated as described below and a dose-dependent relationship between EGF concentration and nuclear translocation of EGFP-Erk1 was found (Fig. 9c,d). Reditribution of GFP fluorescence is expressed in this example as the change in the ratio value between areas in nuclear versus cytoplasmic compartments of the cell. Each time profile is
10   the average of nuclear to cytoplasmic ratios from six cells in each treatment.

EXAMPLE 4:

Probes for detection of Erk2 redistribution.

Useful for monitoring signalling pathways involving MAPK, e.g. to identify compounds which
15   modulate the activity of the pathway in living cells.

Erk2, a serine/threonine protein kinase, is closely related to Erk1 but not identical; it is a component of a signalling pathway which is activated by e.g. many growth factors.

a) The rat Erk2 gene (GenBank Accession number: M64300) was amplified using PCR ac-
20   cording to standard protocols with primers Erk2-top (SEQ ID NO:11) and Erk2-bottom/+stop (SEQ ID NO:13) The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-Erk2 fusion (SEQ ID NO:40 &41) under the control of a CMV promoter.

25   b) The rat Erk2 gene (GenBank Accession number: M64300) was amplified using PCR according to standard protocols with primers (SEQ ID NO:11) Erk2-top and Erk2-bottom/-stop (SEQ ID NO:12). The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produces an Erk2-EGFP fusion (SEQ ID NO:58 &59) under
30   the control of a CMV promoter.

The resulting plasmids were transfected into CHO cells and BHK cells. The cells were grown under standard conditions. Prior to experiments, the cells were starved in medium without serum for 48-72 hours. This led to a predominantly cytoplasmic localization of both probes,

5   especially in BHK cells. 10% fetal calf serum was added to the cells and the fluorescence of the cells was recorded as explained in example 3. Addition of serum caused the probes to redistribute into the nucleus within minutes of addition of serum.

EXAMPLE 5:

10   Probes for detection of Smad2 redistribution.

Useful for monitoring signalling pathways activated by some members of the transforming growth factor-beta family, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Smad 2, a signal transducer, is a component of a signalling pathway which is induced by

15   some members of the TGFbeta family of cytokines.

a) The human Smad2 gene (GenBank Accession number: AF027964) was amplified using PCR according to standard protocols with primers Smad2-top (SEQ ID NO:24) and Smad2-bottom/+stop (SEQ ID NO:26) . The PCR product was digested with restriction enzymes E-

20   coR1 and Acc65I, and ligated into pEGFP-C1 (Clontech; Palo Alto; GenBank Accession number U55763) digested with EcoR1 and Acc65I. This produces an EGFP-Smad2 fusion (SEQ ID NO:50&51) under the control of a CMV promoter.

b) The human Smad2 gene (GenBank Accession number: AF027964) was amplified using PCR according to standard protocols with primers Smad2-top (SEQ ID NO:24) and Smad2-

25   bottom/-stop (SEQ ID NO:25) . The PCR product was digested with restriction enzymes E-coR1 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and Acc65I. This produces a Smad2-EGFP fusion (SEQ ID NO:74 &75) under the control of a CMV promoter.

30   The plasmid containing the EGFP-Smad2 fusion was transfected into HEK293 cells, where it showed a cytoplasmic distribution. Prior to experiments the cells were grown in 8 well Nunc

42

chambers in DMEM with 10% FCS to 80% confluency and starved overnight in HAM F-12 medium without FCS.

For experiments, the HAM F-12 medium was replaced with Hepes buffer pH 7.2.

The experimental setup of the microscope was as described in example 1.

5   90 images were collected with 10 seconds between each, and with the test compound added after image number 5.

After serum starvation of cells, each nucleus contains less GFP fluorescence than the sur- rounding cytoplasm (Fig. 10a). Addition of TGFbeta caused within minutes a redistribution of

10   EGFP-Smad2 from the cytoplasma into the nucleus (Fig. 10b).

The redistribution of fluorescence within the treated cells was quantified simply as the fracti- onal increase in nuclear fluorescence normalised to the starting value of GFP fluorescence in the nucleus of each unstimulated cell.

15   EXAMPLE 6:

Probe for detection of VASP redistribution.

Useful for monitoring signalling pathways involving rearrangement of cytoskeletal elements, e.g. to identify compounds which modulate the activity of the pathway in living cells.

VASP, a phosphoprotein, is a component of cytoskeletal structures, which redistributes in

20   response to signals which affect focal adhesions.

a) The human VASP gene (GenBank Accession number: Z46389) was amplified using PCR according to standard protocols with primers VASP-top (SEQ ID NO:94) and VASP- bottom/+stop (SEQ ID NO:95). The PCR product was digested with restriction enzymes Hind3 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession

25   number U55763) digested with Hind3and BamH1. This produces an EGFP-VASP fusion (SEQ ID NO:124 &125) under the control of a CMV promoter.

The resulting plasmid was transfected into CHO cells expressing the human insulin receptor using the calcium-phosphate transfection method. Prior to experiments, cells were grown in 8 well Nunc chambers and starved overnight in medium without FCS.

43

Experiments are performed in a microscope setup as described in example 1.

10% FCS was added to the cells and images were collected. The EGFP-VASP fusion was redistributed from a somewhat even distribution near the periphery into more localized structures, identified as focal adhesion points (Fig. 11).

5

A large number of further GFP fusions have been made or are in the process of being made, as apparent from the following Examples 7-22 which also suggest suitable host cells and substances for activation of the cellular signalling pathways to be monitored and analyzed.

10

EXAMPLE 7:

Probe for detection of actin redistribution.

15 Useful for monitoring signalling pathways involving rearrangement or formation of actin fila-ments, e.g. to identify compounds which modulate the activity of pathways leading to cyto-skeletal rearrangements in living cells.

Actin is a component of cytoskeletal structures, which redistributes in response to very many cellular signals.

20

The actin binding domain of the human alpha-actinin gene (GenBank Accession number: X15804) was amplified using PCR according to standard protocols with primers ABD-top (SEQ ID NO:90) and ABD-bottom/-stop (SEQ ID NO:91). The PCR product was digested with restriction enzymes Hind3 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto;

25 GenBank Accession number U55762) digested with Hind3 and BamH1. This produced an actin-binding-domain-EGFP fusion (SEQ ID NO:128 &129) under the control of a CMV pro-moter.

The resulting plasmid was transfected into CHO cells expressing the human insulin receptor. Cells were stimulated with insulin which caused the actin binding domain-EGFP probe to be-

30 come redistributed into morphologically distinct membrane-associated structures.

44

Example 8:

Probes for detection of p38 redistribution.

5   Useful for monitoring signalling pathways responding to various cellular stress situations, e.g. to identify compounds which modulate the activity of the pathway in living cells, or as a counterscreen.

p38, a serine/thronine protein kinase, is a component of a stress-induced signalling pathway which is activated by many types of cellular stress, e.g. TNFalpha, anisomycin, UV and mi-
10   tomycin C.

a) The human p38 gene (GenBank Accession number: L35253) was amplified using PCR according to standard protocols with primers p38-top (SEQ ID NO:14) and p38-bottom/+stop (SEQ ID NO: 16). The PCR product was digested with restriction enzymes
15   Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produced an EGFP-p38 fusion (SEQ ID NO:46 &47) under the control of a CMV promoter.

b) The human p38 gene (GenBank Accession number: L35253) was amplified using PCR according to standard protocols with primers p38-top (SEQ ID NO:13) and p38-bottom/-stop
20   (SEQ ID NO:15) . The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produced a p38-EGFP fusion (SEQ ID NO:64 &65) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. HEK293, in which the
25   EGFP-p38 probe and/or the p38-EGFP probe should change its cellular distribution from predominantly cytoplasmic to nuclear within minutes in response to activation of the signal-ling pathway with e.g. anisomycin.

Example 9:

30   Probes for detection of Jnk1 redistribution.

Useful for monitoring signalling pathways responding to various cellular stress situations, e.g. to identify compounds which modulate the activity of the pathway in living cells, or as a counterscreen.

Jnk1, a serine/threonine protein kinase, is a component of a stress-induced signalling pa-
5   thway different from the p38 described above, though it also is activated by many types of cellular stress, e.g. TNFalpha, anisomycin and UV.

a) The human Jnk1 gene (GenBank Accession number: L26318) was amplified using PCR according to standard protocols with primers Jnk-top (SEQ ID NO:17) and Jnk-bottom/+stop
10   (SEQ ID NO:19) . The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produced an EGFP-Jnk1 fusion (SEQ ID NO:44 &45) under the control of a CMV promoter.

b) The human Jnk1 gene (GenBank Accession number: L26318) was amplified using PCR
15   according to standard protocols with primers Jnk-top (SEQ ID NO:17) and Jnk-bottom/-stop (SEQ ID NO:18) . The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produced a Jnk1-EGFP fusion (SEQ ID NO:62 &63) under the control of a CMV promoter.

20   The resulting plasmids are transfected into a suitable cell line, e.g. HEK293, in which the EGFP-Jnk1 probe and/or the Jnk1-EGFP probe should change its cellular distribution from predominantly cytoplasmic to nuclear in response to activation of the signalling pathway with e.g. anisomycin.

25

Example 10:

Probes for detection of PKG redistribution.

Useful for monitoring signalling pathways involving changes in cyclic GMP levels, e.g. to identify compounds which modulate the activity of the pathway in living cells.

30   PGK, a cGMP-dependent serine/threonine protein kinase, mediates the guanylyl-cyclase/cGMP signal.

a) The human PKG gene (GenBank Accession number: Y07512) is amplified using PCR ac-
cording to standard protocols with primers PKG-top (SEQ ID NO:81) and PKG-bottom/+stop
(SEQ ID NO:83) . The PCR product is digested with restriction enzymes Xho1 and BamH1,
5   and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) dige-
sted with Xho1 and BamH1. This produces an EGFP-PKG fusion (SEQ ID NO:134 &135)
under the control of a CMV promoter.

b) The human PKG gene (GenBank Accession number: Y07512) is amplified using PCR ac-
cording to standard protocols with primers PKG-top (SEQ ID NO:81) and PKG-bottom/-stop
10   (SEQ ID NO: 82) . The PCR product is digested with restriction enzymes Xho1 and BamH1,
and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) dige-
sted with Xho1 and BamH1. This produces a PKG-EGFP fusion (SEQ ID NO:136 &137) un-
der the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. A10, in which the EGFP-
15   PKG probe and/or the PKG-EGFP probe should change its cellular distribution from cyto-
plasmic to one associated with cytoskeletal elements within minutes in response to treatment
with agents which raise nitric oxide (NO) levels.

Example 11:

20   Probes for detection of IkappaB kinase redistribution.

Useful for monitoring signalling pathways leading to NFkappaB activation, e.g. to identify
compounds which modulate the activity of the pathway in living cells.

IkappaB kinase, a serine/threonine kinase, is a component of a signalling pathway which is
activated by a variety of inducers including cytokines, lymphokines, growth factors and
25   stress.

a) The alpha subunit of the human IkappaB kinase gene (GenBank Accession number:
AF009225) is amplified using PCR according to standard protocols with primers IKK-top
(SEQ ID NO:96) and IKK-bottom/+stop (SEQ ID NO:98). The PCR product is digested with
30   restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-C1 (Clontech, Palo Alto;

GenBank Accession number U55763) digested with EcoR1and Acc65I. This produces an EGFP-IkappaB-kinase fusion (SEQ ID NO:120 &121) under the control of a CMV promoter.

b) The alpha subunit of the human IkappaB kinase gene (GenBank Accession number: AF009225) is amplified using PCR according to standard protocols with primers IKK-top

5 (SEQ ID NO:96) and IKK-bottom/-stop (SEQ ID NO:97). The PCR product is digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and Acc65I. This produces an IkappaB-kinase-EGFP fusion (SEQ ID NO:122 &123) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the

10 EGFP-IkappaB-kinase probe and/or the IkappaB-kinase-EGFP probe should achieve a more cytoplasmic distribution within seconds following stimulation with e.g. TNFalpha.

Example 12:

Probes for detection of CDK2 redistribution.

15 Useful for monitoring signalling pathways of the cell cycle, e.g. to identify compounds which modulate the activity of the pathway in living cells.

CDK2, a cyclin-dependent serine/threonine kinase, is a component of the signalling system which regulates the cell cycle.

20 a) The human CDK2 gene (GenBank Accession number: X61622) is amplified using PCR according to standard protocols with primers CDK2-top (SEQ ID NO:102) and CDK2-bottom/+stop (SEQ ID NO: 104). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-CDK2 fusion (SEQ ID

25 NO:114 &115) under the control of a CMV promoter.

b) The human CDK2 gene (GenBank Accession number: X61622) is amplified using PCR according to standard protocols with primers CDK2-top (SEQ ID NO:102) and CDK2-bottom/-stop (SEQ ID NO:103). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number

30 U55762) digested with Xho1 and BamH1. This produces a CDK2-EGFP fusion (SEQ ID NO:112 &113) under the control of a CMV promoter.

48

The resulting plasmids are transfected into a suitable cell line, e.g. HEK293 in which the EGFP-CDK2 probe and/or the CDK2-EGFP probe should change its cellular distribution from cytoplasmic in contact-inhibited cells, to nuclear location in response to activation with a number of growth factors, e.g. IGF.

5

Example 13:

Probes for detection of Grk5 redistribution.

Useful for monitoring signalling pathways involving desensitization of G-protein coupled receptors, e.g. to identify compounds which modulate the activity of the pathway in living cells.

10   Grk5, a G-protein coupled receptor kinase, is a component of signalling pathways involving membrane bound G-protein coupled receptors.

a) The human Grk5 gene (GenBank Accession number: L15388) is amplified using PCR according to standard protocols with primers Grk5-top (SEQ ID NO:27) and Grk5-

15   bottom/+stop (SEQ ID NO:29). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Grk5 fusion (SEQ ID NO:42 &43) under the control of a CMV promoter.

b) The human Grk5 gene (GenBank Accession number: L15388) is amplified using PCR according to standard protocols with primers Grk5-top (SEQ ID NO:27) and Grk5-bottom/-stop

20   (SEQ ID NO:28). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produces a Grk5-EGFP fusion (SEQ ID NO:60 &61) under the control of a CMV promoter.

25   The resulting plasmids are transfected into a suitable cell line, e.g. HEK293 expressing a rat dopamine D1A receptor, in which the EGFP-Grk5 probe and/or the Grk5-EGFP probe should change its cellular distribution from predominantly cytoplasmic to peripheral in response to activation of the signalling pathway with e.g. dopamine.

30   Example 14:

49

Probes for detection of Zap70 redistribution.

Useful for monitoring signalling pathways involving the T cell receptor, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Zap70, a tyrosine kinase, is a component of a signalling pathway which is active in e.g. T-cell
5   differentiation.

a) The human Zap70 gene (GenBank Accession number: L05148) is amplified using PCR according to standard protocols with primers Zap70-top (SEQ ID NO:105) and Zap70-bottom/+stop (SEQ ID NO:107). The PCR product is digested with restriction enzymes E-
10   coR1 and BamH1, and ligated into pEGFP-C1 (GenBank Accession number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Zap70 fusion (SEQ ID NO:108 &109) under the control of a CMV promoter.

b) The human Zap70 gene (GenBank Accession number: L05148) is amplified using PCR according to standard protocols with primers Zap70-top (SEQ ID NO:105) and Zap70-
15   bottom/-stop (SEQ ID NO:106). The PCR product is digested with restriction enzymes E-coR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produces a Zap70-EGFP fusion (SEQ ID NO:110 &111) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the
20   EGFP-Zap70 probe and/or the Zap70-EGFP probe should change its cellular distribution from cytoplasmic to membrane-associated within seconds in response to activation of the T cell receptor signalling pathway with e.g. antibodies to CD3epsilon.

Example 15:

25   Probes for detection of p85 redistribution.

Useful for monitoring signalling pathways involving PI-3 kinase, e.g. to identify compounds which modulate the activity of the pathway in living cells.

p85alpha is the regulatory subunit of PI3-kinase which is a component of many pathways involving membrane-bound tyrosine kinase receptors and G-protein-coupled receptors.

30

50

a) The human p85alpha gene (GenBank Accession number: M61906) was amplified using PCR according to standard protocols with primers p85-top-C (SEQ ID NO:22) and p85-bottom/+stop (SEQ ID NO:23) . The PCR product was digested with restriction enzymes Bgl2 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession

5   number U55763) digested with Bgl2 and BamH1. This produced an EGFP-p85alpha fusion (SEQ ID NO:48 &49) under the control of a CMV promoter.

b) The human p85alpha gene (GenBank Accession number: M61906) was amplified using PCR according to standard protocols with primers p85-top-N (SEQ ID NO:20) and p85-bottom/-stop (SEQ ID NO:21) . The PCR product was digested with restriction enzymes E-

10   coR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produced a p85alpha-EGFP fusion (SEQ ID NO:66 &67) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. CHO expressing the human insulin receptor, in which the EGFP-p85 probe and/or the p85-EGFP probe may change

15   its cellular distribution from cytoplasmic to membrane-associated within minutes in response to activation of the receptor with insulin.

Example 16:

Probes for detection of protein-tyrosine phosphatase redistribution.

20   Useful for monitoring signalling pathways involving tyrosine kinases, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Protein-tyrosine phosphatase1C, a tyrosine-specific phosphatase, is an inhibitory component in signalling pathways involving e.g. some growth factors.

25   a) The human protein-tyrosine phosphatase 1C gene (GenBank Accession number: X62055) is amplified using PCR according to standard protocols with primers PTP-top (SEQ ID NO:99) and PTP-bottom/+stop (SEQ ID NO:101). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and EcoR1. This produces an EGFP-PTP

30   fusion (SEQ ID NO:116 &117) under the control of a CMV promoter.

b) The human protein-tyrosine phosphatase 1C gene (GenBank Accession number: X62055) is amplified using PCR according to standard protocols with primers PTP-top (SEQ ID NO:99) and PTP-bottom/-stop (SEQ ID NO:100). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank

5   Accession number U55762) digested with Xho1 and EcoR1. This produces a PTP-EGFP fusion (SEQ ID NO:118 &119) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. MCF-7 in which the EGFP-PTP probe and/or the PTP-EGFP probe should change its cellular distribution from cytoplasm to the plasma menbrane within minutes in response to activation of the growth

10   inhibitory signalling pathway with e.g. somatostatin.

Example 17:

Probes for detection of Smad4 redistribution.

Useful for monitoring signalling pathways involving most members of the transforming

15   growth factor-beta family, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Smad4, a signal transducer, is a common component of signalling pathways induced by various members of the TGFbeta family of cytokines.

20   a) The human Smad4 gene (GenBank Accession number: U44378) was amplified using PCR according to standard protocols with primers Smad4-top and Smad4-bottom/+stop (SEQ ID NO:35) . The PCR product was digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with EcoR1 and BamH1. This produce an EGFP-Smad4 fusion (SEQ ID

25   NO:52 &53) under the control of a CMV promoter.

b) The human Smad4 gene (GenBank Accession number: U44378) was amplified using PCR according to standard protocols with primers Smad4-top (SEQ ID NO:33) and Smad4-bottom/-stop (SEQ ID NO:34). The PCR product was digested with restriction enzymes E-coR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession

30   number U55762) digested with EcoR1 and BamH1. This produced a Smad4-EGFP fusion (SEQ ID NO:76 &77) under the control of a CMV promoter.

52

The resulting plasmids are transfected into a cell line, e.g. HEK293 in which the EGFP-Smad4 probe and/or the Smad4-EGFP probe should change its cellular distribution within minutes from cytoplasmic to nuclear in response to activation of the signalling pathway with e.g. TGFbeta.

5

Example 18:

Probes for detection of Stat5 redistribution.

Useful for monitoring signalling pathways involving the activation of tyrosine kinases of the Jak family, e.g. to identify compounds which modulate the activity of the pathway in living

10   cells.

Stat5, signal transducer and activator of transcription, is a component of signalling pathways which are induced by e.g. many cytokines and growth factors.

a) The human Stat5 gene (GenBank Accession number: L41142) was amplified using PCR

15   according to standard protocols with primers Stat5-top (SEQ ID NO:30) and Stat5-bottom/+stop (SEQ ID NO:32). The PCR product was digested with restriction enzymes Bgl2 and Acc65I, and ligated into pEGFP-C1 (Clontech; Palo Alto; GenBank Accession number U55763) digested with Bgl2 and Acc65I. This produced an EGFP-Stat5 fusion (SEQ ID NO:54 &55) under the control of a CMV promoter.

20   b) The human Stat5 gene (GenBank Accession number: L41142) was amplified using PCR according to standard protocols with primers Stat5-top (SEQ ID NO:30) and Stat5-bottom/-stop (SEQ ID NO:331). The PCR product was digested with restriction enzymes Bgl2 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Bgl2 and Acc65I. This produced a Stat5-EGFP fusion (SEQ ID NO:78

25   &79) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. MIN6 in which the EGFP-Stat5 probe and/or the Stat5-EGFP probe should change its cellular distribution from cyto-plasmic to nuclear within minutes in response to activation signalling pathway with e.g. pro-lactin.

30

53

Example 19:

Probes for detection of NFAT redistribution.

Useful for monitoring signalling pathways involving activation of NFAT, e.g. to identify compounds which modulate the activity of the pathway in living cells.

5   NFAT, an activator of transcription, is a component of signalling pathways which is involved in e.g. immune responses.

a) The human NFAT1 gene (GenBank Accession number: U43342) is amplified using PCR according to standard protocols with primers NFAT-top (SEQ ID NO:84) and NFAT-

10   bottom/+stop (SEQ ID NO:86). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and EcoR1. This produces an EGFP-NFAT fusion (SEQ ID NO:130 &131) under the control of a CMV promoter.

b) The human NFAT gene (GenBank Accession number: U43342) is amplified using PCR

15   according to standard protocols with primers NFAT-top (SEQ ID NO:84) and NFAT-bottom/-stop (SEQ ID NO:85). The PCR product is digested with restriction enzymes Xho1 and E-coR1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and EcoR1. This produces an NFAT-EGFP fusion (SEQ ID NO:132 &133) under the control of a CMV promoter.

20   The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-NFAT probe and/or the NFAT-EGFP probe should change its cellular distribution from cytoplasmic to nuclear within minutes in response to activation of the signalling pathway with e.g. antibodies to CD3epsilon.

25   Example 20:

Probes for detection of NFkappaB redistribution.

Useful for monitoring signalling pathways leading to activation of NFkappaB, e.g. to identify compounds which modulate the activity of the pathway in living cells.

SUBSTITUTE SHEET (RULE 26)

54

NFkappaB, an activator of transcription, is a component of signalling pathways which are responsive to a varity of inducers including cytokines, lymphokines, some immunosuppressive agents.

5   a) The human NFkappaB p65 subunit gene (GenBank Accession number: M62399) is amplified using PCR according to standard protocols with primers NFkappaB-top (SEQ ID NO:87) and NFkappaB-bottom/+stop (SEQ ID NO:89). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an
10   EGFP-NFkappaB fusion (SEQ ID NO:142 & 143) under the control of a CMV promoter.

b) The human NFkappaB p65 subunit gene (GenBank Accession number: M62399) is amplified using PCR according to standard protocols with primers NFkappaB-top (SEQ ID NO:87) and NFkappaB-bottom/-stop (SEQ ID NO:88). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; Gen-
15   Bank Accession number U55762) digested with Xho1 and BamH1. This produces an NFkappaB-EGFP fusion (SEQ ID NO:140 & 141) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-NFkappaB probe and/or the NFkappaB-EGFP probe should change its cellular distribution from cytoplasmic to nuclear in response to activation of the signalling pathway with
20   e.g. TNFalpha.

Example 21:

Probe for detection of RhoA redistribution.

Useful for monitoring signalling pathways involving RhoA, e.g. to identify compounds which
25   modulate the activity of the pathway in living cells.

RhoA, a small GTPase, is a component of many signalling pathways, e.g. LPA induced cytoskeletal rearrangements.

The human RhoA gene (GenBank Accession number: L25080) was amplified using PCR
30   according to standard protocols with primers RhoA-top (SEQ ID NO:92) and RhoA-bottom/+stop (SEQ ID NO:93). The PCR product was digested with restriction enzymes

SUBSTITUTE SHEET (RULE 26)

55

Hind3 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Hind3and BamH1. This produced an EGFP-RhoA fusion (SEQ ID NO:126 &127) under the control of a CMV promoter.

5   The resulting plasmid is transfected into a suitable cell line, e.g. Swiss3T3, in which the EGFP-RhoA probe should change its cellular distribution from a reasonably homogenous to a peripheral distribution within minutes of activation of the signalling pathway with e.g. LPA.

Example 22:

Probes for detection of PKB redistribution.

Useful for monitoring signalling pathways involving PKB e.g. to identify compounds which
10   modulate the activity of the pathway in living cells.

PKB, a serine/threonine kinase, is a component in various signalling pathways, many of which are activated by growth factors.

a) The human PKB gene (GenBank Accession number: M63167) is amplified using PCR ac-
15   cording to standard protocols with primers PKB-top (SEQ ID NO:36) and PKB-bottom/+stop (SEQ ID NO:80) . The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) dige-sted with Xho1 and BamH1. This produces an EGFP-PKB fusion (SEQ ID NO:138 & 139) under the control of a CMV promoter.

20   b) The human PKB gene (GenBank Accession number: M63167) was amplified using PCR according to standard protocols with primers PKB-top (SEQ ID NO:36) and PKB-bottom/-stop (SEQ ID NO:37) . The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produced a PKB-EGFP fusion (SEQ ID
25   NO:70 &71) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. CHO expressing the human insulin receptor, in which the EGFP-PKB probe and/or the PKB-EGFP probe cycles between cytoplasmic and membrane locations during the activation-deactivation process following addition of insulin. The transition should be apparent within minutes.

REFERENCES:

Adams, S.R., Harootunian, A.T., Buechler, Y.J., Taylor, S.S. & Tsien, R.Y. (1991) Nature **349**, 694-697

5 Blobe, G.C., Stribling, D.S., Fabbro, D., Stabel, S & Hannun, Y.A. (1996) J. Biol. Chem. **271**, 15823-15830

Chalfie, M., Tu, Y., Euskirchen, G., Ward, W.W. & Prasher, D.C. (1994) Science **263**, 802-805

Cossette, L.J., Hoglinger, O., Mou, L.J. & Shen, S.H. (1997) Exp. Cell Res. **223**, 459-466

10 DeBernardi, M.A. & Brooker, G. (1996) Proc. Natl. Acad. Sci. USA **93**, 4577-4582

Farese, R.V.. (1992) Biochem. J. **288**, 319-323

Fulop Jr., T., Leblanc, C., Lacombe, G. & Dupuis, G. (1995) FEBS Lett. **375**, 69-74

Godson, C., Masliah, E., Balboa, M.A., Ellisman, M.H. & Insel, P.A. (1996) Biochem. Biophys. Acta **1313**, 63-71

15 Khalil, R.A., Lajoie, C., Resnick, M.S. & Morgan, K.G. (1992) American Physiol. Society **c**, 714-719

Sano, M., Kohno, M. & Iwanaga, M. (1995) Brain Res. **688**, 213-218

Bastiaens, P.I.H. & Jovin, T.M. (1996) Proc. Natl. Acad. Sci. USA **93**, 8407-8412

Schmidt, D.J., Ikebe, M., Kitamura, K., & Fay, F.S. (1997) FASEB J. **11**, 2924 (Abstract)

20 Sakai, N., Sasaki, K., Hasegawa, C., Ohkura, M., Suminka, K., Shirai, Y. & Saito, N. (1996) Soc. Neuroscience **22**, 69P (Abstract)

Sakai, N., Sakai, K. Hasegawa, C., Ohkura, M., Sumioka, ., Shirai, Y., & Naoaki, S. (1997) Japanese Journal of Pharmacology **73**, 69P (Abstract of a meeting held 22-23 March)

SEQUENCE LISTING

5   (1) GENERAL INFORMATION

         (i) APPLICANT: NovoNordisk, BioImage

         (ii) TITLE OF THE INVENTION: A Method of Detecting Cellular
10   Translocation of Biologically Active Polypeptides Using
                        Fluorescense Imaging

         (iii) NUMBER OF SEQUENCES: 143

15   (iv) CORRESPONDENCE ADDRESS:
             (A) ADDRESSEE: NovoNordisk, BioImage
             (B) STREET: Mørkhøjbygade 28
             (C) CITY: Søborg
             (D) STATE: DK
20   (E) COUNTRY: DENMARK
             (F) ZIP: 2860

         (v) COMPUTER READABLE FORM:
             (A) MEDIUM TYPE: Diskette
25   (B) COMPUTER: IBM Compatible
             (C) OPERATING SYSTEM: DOS
             (D) SOFTWARE: FastSEQ for Windows Version 2.0

30   (viii) ATTORNEY/AGENT INFORMATION:
             (A) NAME: , PV&P R
             (B) REGISTRATION NUMBER:
             (C) REFERENCE/DOCKET NUMBER:

35
         (2) INFORMATION FOR SEQ ID NO:1:

         (i) SEQUENCE CHARACTERISTICS:
             (A) LENGTH: 53 base pairs
40   (B) TYPE: nucleic acid
             (C) STRANDEDNESS: single
             (D) TOPOLOGY: linear

45   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

    TTGGACACAA GCTTTGGACA CGGCGCGCCA TGAGTAAAGG AGAAGAACTT TTC   53

         (2) INFORMATION FOR SEQ ID NO:2:
50
         (i) SEQUENCE CHARACTERISTICS:
             (A) LENGTH: 53 base pairs
             (B) TYPE: nucleic acid
             (C) STRANDEDNESS: single
55   (D) TOPOLOGY: linear

SUBSTITUTE SHEET (RULE 26)

58

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

GTCATCTTCT CGAGTCTTAC TCCTGAGGTT TGTATAGTTC ATCCATGCCA TGT   53

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
  (A) LENGTH: 54 base pairs
  (B) TYPE: nucleic acid
  (C) STRANDEDNESS: single
  (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

TTGGACACAA GCTTTGGACA CCCTCAGGAT ATGGGCAACG CCGCCGCCGC CAAG   54

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
  (A) LENGTH: 55 base pairs
  (B) TYPE: nucleic acid
  (C) STRANDEDNESS: single
  (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

GTCATCTTCT CGAGTCTTTC AGGCGCGCCC AAACTCAGTA AACTCCTTGC CACAC   55

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
  (A) LENGTH: 55 base pairs
  (B) TYPE: nucleic acid
  (C) STRANDEDNESS: single
  (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

TTGGACACAA GCTTTGGACA CCCTCAGGAT ATGGCTGACG TTTACCCGGC CAACG   55

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
  (A) LENGTH: 55 base pairs
  (B) TYPE: nucleic acid
  (C) STRANDEDNESS: single
  (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

GTCATCTTCT CGAGTCTTTC AGGCGCGCCC TACTGCACTT TGCAAGATTG GGTGC   55

58

SUBSTITUTE SHEET (RULE 26)

(2) INFORMATION FOR SEQ ID NO:7:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 64 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

TTGGACACAA GCTTTGGACA CCCTCAGGAT ATGGCGGCGG CGGCGGCGGC TCCGGGGGGC   60
GGGG   64

(2) INFORMATION FOR SEQ ID NO:8:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 55 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

GTCATCTTCT CGAGTCTTTC AGGCGCGCCC GGGGCCCTCT GGCGCCCCTG GCTGG   55

(2) INFORMATION FOR SEQ ID NO:9:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 30 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

TAGAATTCAA CCATGGCGGC GGCGGCGGCG   30

(2) INFORMATION FOR SEQ ID NO:10:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 29 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

TAGGATCCCT AGGGGGCCTC CAGCACTCC   29

(2) INFORMATION FOR SEQ ID NO:11:

60

```
        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 31 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
 5          (D) TOPOLOGY: linear


        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

10  TACTCGAGTA ACCATGGCGG CGGCGGCGGC G                              31


            (2) INFORMATION FOR SEQ ID NO:12:


        (i) SEQUENCE CHARACTERISTICS:
15          (A) LENGTH: 25 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear


20
        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

    TAGGATCCAT AGATCTGTAT CCTGG                                     25


25          (2) INFORMATION FOR SEQ ID NO:13:


        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 26 base pairs
            (B) TYPE: nucleic acid
30          (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear


        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:
35
    TAGGATCCTT AAGATCTGTA TCCTGG                                    26


            (2) INFORMATION FOR SEQ ID NO:14:


40      (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 28 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear
45


        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

    ATCTCGAGGG AAAATGTCTC AGGAGAGG                                  28
50
            (2) INFORMATION FOR SEQ ID NO:15:


        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 28 base pairs
55          (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
```

60

61

(D) TOPOLOGY: linear

5   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ATGGATCCTC GGACTCCATC TCTTCTTG   28

         (2) INFORMATION FOR SEQ ID NO:16:

10   (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 29 base pairs
         (B) TYPE: nucleic acid
         (C) STRANDEDNESS: single
         (D) TOPOLOGY: linear

15

         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

ATGGATCCTC AGGACTCCAT CTCTTCTTG   29

20   (2) INFORMATION FOR SEQ ID NO:17:

         (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 28 base pairs
25   (B) TYPE: nucleic acid
         (C) STRANDEDNESS: single
         (D) TOPOLOGY: linear

30   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

GTCTCGAGCC ATCATGAGCA GAAGCAAG   28

         (2) INFORMATION FOR SEQ ID NO:18:
35

         (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 27 base pairs
         (B) TYPE: nucleic acid
         (C) STRANDEDNESS: single
40   (D) TOPOLOGY: linear

         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

45   GTGGATCCCA CTGCTGCACC TGTGCTA   27

         (2) INFORMATION FOR SEQ ID NO:19:

         (i) SEQUENCE CHARACTERISTICS:
50   (A) LENGTH: 28 base pairs
         (B) TYPE: nucleic acid
         (C) STRANDEDNESS: single
         (D) TOPOLOGY: linear

55

         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

SUBSTITUTE SHEET (RULE 26)

GTGGATCCTC ACTGCTGCAC CTGTGCTA   28

     (2) INFORMATION FOR SEQ ID NO:20:

5

       (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 40 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single

10   (D) TOPOLOGY: linear

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

15 CGCGAATTCC GCCACCATGA GTGCTGAGGG GTACCAGTAC   40

     (2) INFORMATION FOR SEQ ID NO:21:

       (i) SEQUENCE CHARACTERISTICS:

20   (A) LENGTH: 32 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

25

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

CGCGGATCCT GTCGCCTCTG CTGTGCATAT AC   32

30   (2) INFORMATION FOR SEQ ID NO:22:

       (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 30 base pairs
        (B) TYPE: nucleic acid

35   (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

      (vi) ORIGINAL SOURCE:
        (A) ORGANISM: p85-top-C

40

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

GGGAGATCTA TGAGTGCTGA GGGGTACCAG   30

45   (2) INFORMATION FOR SEQ ID NO:23:

       (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 34 base pairs
        (B) TYPE: nucleic acid

50   (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

55
GGGCGGATCC TCATCGCCTC TGCTGTGCAT ATAC   34

(2) INFORMATION FOR SEQ ID NO:24:

5
(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 33 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

10
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

GTGAATTCGA CCATGTCGTC CATCTTGCCA TTC   33

15   (2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 31 base pairs
    (B) TYPE: nucleic acid
20 (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:
25
GTGGTACCCA TGACATGCTT GAGCAACGCA C   31

            (2) INFORMATION FOR SEQ ID NO:26:

30
(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 32 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear
35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

GTGGTACCTT ATGACATGCT TGAGCAACGC AC   32
40
            (2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 31 base pairs
45 (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

50   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

GTGAATTCGT CAATGGAGCT GGAAAACATC G   31

            (2) INFORMATION FOR SEQ ID NO:28:
55
(i) SEQUENCE CHARACTERISTICS:

63

SUBSTITUTE SHEET (RULE 26)

64

       (A) LENGTH: 30 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

5

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

GTGGATCCCT GCTGCTTCCG GTGGAGTTCG   30

10

      (2) INFORMATION FOR SEQ ID NO:29:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 31 base pairs
15   (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

20   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

GTGGATCCCT AGCTGCTTCC GGTGGAGTTC G   31

      (2) INFORMATION FOR SEQ ID NO:30:

25

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 32 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
30   (D) TOPOLOGY: linear

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

35 GTAGATCTAC CATGGCGGGC TGGATCCAGG CC   32

      (2) INFORMATION FOR SEQ ID NO:31:

    (i) SEQUENCE CHARACTERISTICS:
40   (A) LENGTH: 31 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

45

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

GTGGTACCCA TGAGAGGGAG CCTCTGGCAG A   31

50   (2) INFORMATION FOR SEQ ID NO:32:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 31 base pairs
       (B) TYPE: nucleic acid
55   (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

64

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

GTGGTACCTC ATGAGAGGGA GCCTCTGGCA G   31

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 33 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

GTGAATTCAA CCATGGACAA TATGTCTATT ACG   33

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 31 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

GTGGATCCCA GTCTAAAGGT TGTGGGTCTG C   31

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 32 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

GTGGATCCTC AGTCTAAAGG TTGTGGGTCT GC   32

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 27 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

SUBSTITUTE SHEET (RULE 26)

GTCTCGAGGC ACCATGAGCG ACGTGGC   27

       (2) INFORMATION FOR SEQ ID NO:37:

        (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 27 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

TGGGATCCGA GGCCGTGCTG CTGGCCG   27

       (2) INFORMATION FOR SEQ ID NO:38:

        (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 1896 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: cDNA
        (ix) FEATURE:

          (A) NAME/KEY: Coding Sequence
          (B) LOCATION: 1...1891
          (D) OTHER INFORMATION:

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG   48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1   5   10   15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC   96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20   25   30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC   144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
            35   40   45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC   192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
        50   55   60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG   240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65   70   75   80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG   288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85   90   95

BNSDOCID: <WO___9845704A2_I_>

```
     CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG    336
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
             100                 105                 110

 5   GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC    384
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
             115                 120                 125

     ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC    432
10   Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
             130                 135                 140

     AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC    480
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
15   145                 150                 155                 160

     GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC    528
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                         165                 170                 175
20
     GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC    576
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
             180                 185                 190

25   CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
             195                 200                 205

     AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
30   Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
             210                 215                 220

     GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
35   225                 230                 235                 240

     GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCA ACC ATG GCG GCG GCG    768
     Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ala Ala Ala
                         245                 250                 255
40
     GCG GCT CAG GGG GGC GGG GGC GGG GAG CCC CGT AGA ACC GAG GGG GTC    816
     Ala Ala Gln Gly Gly Gly Gly Gly Glu Pro Arg Arg Thr Glu Gly Val
                         260                 265                 270

45   GGC CCG GGG GTC CCG GGG GAG GTG GAG ATG GTG AAG GGG CAG CCG TTC    864
     Gly Pro Gly Val Pro Gly Glu Val Glu Met Val Lys Gly Gln Pro Phe
                         275                 280                 285

     GAC GTG GGC CCG CGC TAC ACG CAG TTG CAG TAC ATC GGC GAG GGC GCG    912
50   Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr Ile Gly Glu Gly Ala
             290                 295                 300

     TAC GGC ATG GTC AGC TCG GCC TAT GAC CAC GTG CGC AAG ACT CGC GTG    960
     Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val Arg Lys Thr Arg Val
55   305                 310                 315                 320
```

SUBSTITUTE SHEET (RULE 26)

68

```
        GCC ATC AAG AAG ATC AGC CCC TTC GAA CAT CAG ACC TAC TGC CAG CGC     1008
        Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln Arg
                        325             330                 335

  5     ACG CTC CGG GAG ATC CAG ATC CTG CTG CGC TTC CGC CAT GAG AAT GTC     1056
        Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe Arg His Glu Asn Val
                        340             345                 350

 10     ATC GGC ATC CGA GAC ATT CTG CGG GCG TCC ACC CTG GAA GCC ATG AGA     1104
        Ile Gly Ile Arg Asp Ile Leu Arg Ala Ser Thr Leu Glu Ala Met Arg
                        355             360                 365

        GAT GTC TAC ATT GTG CAG GAC CTG ATG GAG ACT GAC CTG TAC AAG TTG     1152
        Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys Leu
 15             370             375                 380

        CTG AAA AGC CAG CAG CTG AGC AAT GAC CAT ATC TGC TAC TTC CTC TAC     1200
        Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile Cys Tyr Phe Leu Tyr
        385             390                 395                 400
 20
        CAG ATC CTG CGG GGC CTC AAG TAC ATC CAC TCC GCC AAC GTG CTC CAC     1248
        Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu His
                        405             410                 415

 25     CGA GAT CTA AAG CCC TCC AAC CTG CTC AGC AAC ACC ACC TGC GAC CTT     1296
        Arg Asp Leu Lys Pro Ser Asn Leu Leu Ser Asn Thr Thr Cys Asp Leu
                        420             425                 430

        AAG ATT TGT GAT TTC GGC CTG GCC CGG ATT GCC GAT CCT GAG CAT GAC     1344
 30     Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala Asp Pro Glu His Asp
                        435             440                 445

        CAC ACC GGC TTC CTG ACG GAG TAT GTG GCT ACG CGC TGG TAC CGG GCC     1392
        His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg Ala
 35             450             455                 460

        CCA GAG ATC ATG CTG AAC TCC AAG GGC TAT ACC AAG TCC ATC GAC ATC     1440
        Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp Ile
        465             470                 475                 480
 40
        TGG TCT GTG GGC TGC ATT CTG GCT GAG ATG CTC TCT AAC CGG CCC ATC     1488
        Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro Ile
                        485             490                 495

 45     TTC CCT GGC AAG CAC TAC CTG GAT CAG CTC AAC CAC ATT CTG GGC ATC     1536
        Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly Ile
                        500             505                 510

        CTG GGC TCC CCA TCC CAG GAG GAC CTG AAT TGT ATC ATC AAC ATG AAG     1584
 50     Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Met Lys
                        515             520                 525

        GCC CGA AAC TAC CTA CAG TCT CTG CCC TCC AAG ACC AAG GTG GCT TGG     1632
        Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys Thr Lys Val Ala Trp
 55             530             535                 540
```

SUBSTITUTE SHEET (RULE 26)

```
GCC AAG CTT TTC CCC AAG TCA GAC TCC AAA GCC CTT GAC CTG CTG GAC    1680
Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala Leu Asp Leu Leu Asp
545             550             555             560

CGG ATG TTA ACC TTT AAC CCC AAT AAA CGG ATC ACA GTG GAG GAA GCG    1728.
Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile Thr Val Glu Glu Ala
            565             570             575

CTG GCT CAC CCC TAC CTG GAG CAG TAC TAT GAC CCG ACG GAT GAG CCA    1776
Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Thr Asp Glu Pro
        580             585             590

GTG GCC GAG GAG CCC TTC ACC TTC GCC ATG GAG CTG GAT GAC CTA CCT    1824
Val Ala Glu Glu Pro Phe Thr Phe Ala Met Glu Leu Asp Asp Leu Pro
        595             600             605

AAG GAG CGG CTG AAG GAG CTC ATC TTC CAG GAG ACA GCA CGC TTC CAG    1872
Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu Thr Ala Arg Phe Gln
        610             615             620

CCC GGA GTG CTG GAG GCC C CCTAG                                     1896
Pro Gly Val Leu Glu Ala Pro
625             630
```

(2) INFORMATION FOR SEQ ID NO:39:

    (i) SEQUENCE CHARACTERISTICS:
      (A) LENGTH: 631 amino acids
      (B) TYPE: amino acid
      (C) STRANDEDNESS: single
      (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: protein
    (v) FRAGMENT TYPE: internal

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1               5               10              15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20              25              30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35              40              45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
        50              55              60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65              70              75              80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
            85              90              95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100             105             110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115             120             125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
        130             135             140
```

BNSDOCID: <WO___9845704A2_I_>

70

```
      Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
      145             150             155             160
      Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                      165             170             175
  5   Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                      180             185             190
      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                      195             200             205
      Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
 10   210             215             220
      Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
      225             230             235             240
      Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ala Ala Ala
                      245             250             255
 15   Ala Ala Gln Gly Gly Gly Gly Glu Pro Arg Arg Thr Glu Gly Val
                      260             265             270
      Gly Pro Gly Val Pro Gly Glu Val Glu Met Val Lys Gly Gln Pro Phe
                      275             280             285
      Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr Ile Gly Glu Gly Ala
 20   290             295             300
      Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val Arg Lys Thr Arg Val
      305             310             315             320
      Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln Arg
                      325             330             335
 25   Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe Arg His Glu Asn Val
                      340             345             350
      Ile Gly Ile Arg Asp Ile Leu Arg Ala Ser Thr Leu Glu Ala Met Arg
                      355             360             365
      Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys Leu
 30   370             375             380
      Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile Cys Tyr Phe Leu Tyr
      385             390             395             400
      Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu His
                      405             410             415
 35   Arg Asp Leu Lys Pro Ser Asn Leu Leu Ser Asn Thr Thr Cys Asp Leu
                      420             425             430
      Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala Asp Pro Glu His Asp
                      435             440             445
      His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg Ala
 40   450             455             460
      Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp Ile
      465             470             475             480
      Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro Ile
                      485             490             495
 45   Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly Ile
                      500             505             510
      Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Met Lys
                      515             520             525
      Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys Thr Lys Val Ala Trp
 50   530             535             540
      Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala Leu Asp Leu Leu Asp
      545             550             555             560
      Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile Thr Val Glu Glu Ala
                      565             570             575
 55   Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Thr Asp Glu Pro
                      580             585             590
```

SUBSTITUTE SHEET (RULE 26)

71

```
Val Ala Glu Glu Pro Phe Thr Phe Ala Met Glu Leu Asp Asp Leu Pro
        595                 600                 605
Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu Thr Ala Arg Phe Gln
        610                 615                 620
```
5
```
Pro Gly Val Leu Glu Ala Pro
625                 630
```

        (2) INFORMATION FOR SEQ ID NO:40:

10   (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 1818 base pairs
                (B) TYPE: nucleic acid
                (C) STRANDEDNESS: single
                (D) TOPOLOGY: linear
15
            (ii) MOLECULE TYPE: cDNA
            (ix) FEATURE:

                (A) NAME/KEY: Coding Sequence
20   (B) LOCATION: 1...1815
                (D) OTHER INFORMATION:

            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

25 ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG   48
    Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
     1   5   10   15

    GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC   96
30 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                    20   25   30

    GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC   144
    Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
35   35   40   45

    TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC   192
    Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                    50   55   60
40
    CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG   240
    Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
    65   70   75   80

45 CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG   288
    Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                    85   90   95

    CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG   336
50 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100   105   110

    GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC   384
    Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
55   115   120   125
```

71

```
     ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
         130                 135                 140

 5   AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160

10   GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                     165                 170                 175

     GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
15                   180                 185                 190

     CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                 195                 200                 205
20
     AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
         210                 215                 220

25   GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240

     GGA CTC AGA TCT CGA GTA ACC ATG GCG GCG GCG GCG GCG GCG GGC CCG     768
30   Gly Leu Arg Ser Arg Val Thr Met Ala Ala Ala Ala Ala Ala Gly Pro
                     245                 250                 255

     GAG ATG GTC CGC GGG CAG GTG TTC GAC GTG GGG CCG CGC TAC ACT AAT     816
     Glu Met Val Arg Gly Gln Val Phe Asp Val Gly Pro Arg Tyr Thr Asn
35                   260                 265                 270

     CTC TCG TAC ATC GGA GAA GGC GCC TAC GGC ATG GTT TGT TCT GCT TAT     864
     Leu Ser Tyr Ile Gly Glu Gly Ala Tyr Gly Met Val Cys Ser Ala Tyr
                 275                 280                 285
40
     GAT AAT CTC AAC AAA GTT CGA GTT GCT ATC AAG AAA ATC AGT CCT TTT     912
     Asp Asn Leu Asn Lys Val Arg Val Ala Ile Lys Lys Ile Ser Pro Phe
         290                 295                 300

45   GAG CAC CAG ACC TAC TGT CAG AGA ACC CTG AGA GAG ATA AAA ATC CTA     960
     Glu His Gln Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Lys Ile Leu
     305                 310                 315                 320

     CTG CGC TTC AGA CAT GAG AAC ATC ATC GGC ATC AAT GAC ATC ATC CGG    1008
50   Leu Arg Phe Arg His Glu Asn Ile Ile Gly Ile Asn Asp Ile Ile Arg
                     325                 330                 335

     GCA CCA ACC ATT GAG CAG ATG AAA GAT GTA TAT ATA GTA CAG GAC CTC    1056
     Ala Pro Thr Ile Glu Gln Met Lys Asp Val Tyr Ile Val Gln Asp Leu
55                   340                 345                 350
```

SUBSTITUTE SHEET (RULE 26)

```
     ATG GAG ACA GAT CTT TAC AAG CTC TTG AAG ACA CAG CAC CTC AGC AAT    1104
     Met Glu Thr Asp Leu Tyr Lys Leu Leu Lys Thr Gln His Leu Ser Asn
             355                 360                 365

 5   GAT CAT ATC TGC TAT TTT CTT TAT CAG ATC CTG AGA GGA TTA AAG TAT    1152
     Asp His Ile Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr
             370                 375                 380

     ATA CAT TCA GCT AAT GTT CTG CAC CGT GAC CTC AAG CCT TCC AAC CTC    1200
10   Ile His Ser Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu
     385                 390                 395                 400

     CTG CTG AAC ACC ACT TGT GAT CTC AAG ATC TGT GAC TTT GGC CTT GCC    1248
     Leu Leu Asn Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala
15                       405                 410                 415

     CGT GTT GCA GAT CCA GAC CAT GAT CAT ACA GGG TTC TTG ACA GAG TAT    1296
     Arg Val Ala Asp Pro Asp His Asp His Thr Gly Phe Leu Thr Glu Tyr
                     420                 425                 430
20
     GTA GCC ACG CGT TGG TAC AGA GCT CCA GAA ATT ATG TTG AAT TCC AAG    1344
     Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys
                 435                 440                 445

25   GGT TAT ACC AAG TCC ATT GAT ATT TGG TCT GTG GGC TGC ATC CTG GCA    1392
     Gly Tyr Thr Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala
             450                 455                 460

     GAG ATG CTA TCC AAC AGG CCT ATC TTC CCA GGA AAG CAT TAC CTT GAC    1440
30   Glu Met Leu Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp
     465                 470                 475                 480

     CAG CTG AAT CAC ATC CTG GGT ATT CTT GGA TCT CCA TCA CAG GAA GAT    1488
     Gln Leu Asn His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp
35                   485                 490                 495

     CTG AAT TGT ATA ATA AAT TTA AAA GCT AGA AAC TAT TTG CTT TCT CTC    1536
     Leu Asn Cys Ile Ile Asn Leu Lys Ala Arg Asn Tyr Leu Leu Ser Leu
                     500                 505                 510
40
     CCG CAC AAA AAT AAG GTG CCG TGG AAC AGG TTG TTC CCA AAC GCT GAC    1584
     Pro His Lys Asn Lys Val Pro Trp Asn Arg Leu Phe Pro Asn Ala Asp
             515                 520                 525

45   TCC AAA GCT CTG GAT TTA CTG GAT AAA ATG TTG ACA TTT AAC CCT CAC    1632
     Ser Lys Ala Leu Asp Leu Leu Asp Lys Met Leu Thr Phe Asn Pro His
             530                 535                 540

     AAG AGG ATT GAA GTT GAA CAG GCT CTG GCC CAC CCG TAC CTG GAG CAG    1680
50   Lys Arg Ile Glu Val Glu Gln Ala Leu Ala His Pro Tyr Leu Glu Gln
     545                 550                 555                 560

     TAT TAT GAC CCA AGT GAT GAG CCC ATT GCT GAA GCA CCA TTC AAG TTT    1728
     Tyr Tyr Asp Pro Ser Asp Glu Pro Ile Ala Glu Ala Pro Phe Lys Phe
55                   565                 570                 575
```

SUBSTITUTE SHEET (RULE 26)

```
GAC ATG GAG CTG GAC GAC TTA CCT AAG GAG AAG CTC AAA GAA CTC ATT    1776
Asp Met Glu Leu Asp Asp Leu Pro Lys Glu Lys Leu Lys Glu Leu Ile
            580                 585                 590
```

5
```
TTT GAA GAG ACT GCT CGA TTC CAG CCA GGA TAC AGA TCT TAA            1818
Phe Glu Glu Thr Ala Arg Phe Gln Pro Gly Tyr Arg Ser
            595                 600                 605
```

10   (2) INFORMATION FOR SEQ ID NO:41:

            (i) SEQUENCE CHARACTERISTICS:
                 (A) LENGTH: 605 amino acids
                 (B) TYPE: amino acid
15   (C) STRANDEDNESS: single
                 (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: protein
            (v) FRAGMENT TYPE: internal
20
            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

```
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
     1               5                   10                  15
25   Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                 20                  25                  30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                 35                  40                  45
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
30       50                  55                  60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                     85                  90                  95
35   Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                 100                 105                 110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                 115                 120                 125
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
40       130                 135                 140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                     165                 170                 175
45   Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                 180                 185                 190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                 195                 200                 205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
50       210                 215                 220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240
     Gly Leu Arg Ser Arg Val Thr Met Ala Ala Ala Ala Ala Gly Pro
                     245                 250                 255
55   Glu Met Val Arg Gly Gln Val Phe Asp Val Gly Pro Arg Tyr Thr Asn
                 260                 265                 270
```

```
Leu Ser Tyr Ile Gly Glu Gly Ala Tyr Gly Met Val Cys Ser Ala Tyr
        275                     280                 285
Asp Asn Leu Asn Lys Val Arg Val Ala Ile Lys Lys Ile Ser Pro Phe
        290                     295                 300
Glu His Gln Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Lys Ile Leu
305             310             315                     320
Leu Arg Phe Arg His Glu Asn Ile Ile Gly Ile Asn Asp Ile Ile Arg
                325                 330                 335
Ala Pro Thr Ile Glu Gln Met Lys Asp Val Tyr Ile Val Gln Asp Leu
            340                 345                 350
Met Glu Thr Asp Leu Tyr Lys Leu Leu Lys Thr Gln His Leu Ser Asn
        355                 360                 365
Asp His Ile Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr
        370                 375                 380
Ile His Ser Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu
385                 390                 395                 400
Leu Leu Asn Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala
                405                 410                 415
Arg Val Ala Asp Pro Asp His Asp His Thr Gly Phe Leu Thr Glu Tyr
            420                 425                 430
Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys
            435                 440                 445
Gly Tyr Thr Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala
    450                 455                 460
Glu Met Leu Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp
465                 470                 475                 480
Gln Leu Asn His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp
            485                 490                 495
Leu Asn Cys Ile Ile Asn Leu Lys Ala Arg Asn Tyr Leu Leu Ser Leu
            500                 505                 510
Pro His Lys Asn Lys Val Pro Trp Asn Arg Leu Phe Pro Asn Ala Asp
        515                 520                 525
Ser Lys Ala Leu Asp Leu Leu Asp Lys Met Leu Thr Phe Asn Pro His
        530                 535                 540
Lys Arg Ile Glu Val Glu Gln Ala Leu Ala His Pro Tyr Leu Glu Gln
545                 550                 555                 560
Tyr Tyr Asp Pro Ser Asp Glu Pro Ile Ala Glu Ala Pro Phe Lys Phe
                565                 570                 575
Asp Met Glu Leu Asp Asp Leu Pro Lys Glu Lys Leu Lys Glu Leu Ile
            580                 585                 590
Phe Glu Glu Thr Ala Arg Phe Gln Pro Gly Tyr Arg Ser
        595                 600                 605
```

(2) INFORMATION FOR SEQ ID NO:42:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 2529 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA
    (ix) FEATURE:

        (A) NAME/KEY: Coding Sequence
        (B) LOCATION: 1...2526

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

```
 5   ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG    48
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                  10                  15

     GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC    96
10   Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                    20                  25                  30

     GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC   144
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
15                  35                  40                  45

     TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC   192
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                 50                  55                  60
20
     CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG   240
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80

25   CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG   288
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                     85                  90                  95

     CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG   336
30   Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100                 105                 110

     GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC   384
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
35                  115                 120                 125

     ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC   432
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                130                 135                 140
40
     AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC   480
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160

45   GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC   528
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                    165                 170                 175

     GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC   576
50   Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                    180                 185                 190

     CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG   624
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
55                  195                 200                 205
```

SUBSTITUTE SHEET (RULE 26)

77

```
      AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
      Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
          210             215             220

  5   GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
      Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
      225             230             235             240

 10   GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG TCA ATG GAG CTG GAA      768
      Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ser Met Glu Leu Glu
                  245             250             255

      AAC ATC GTG GCC AAC ACG GTC TTG CTG AAA GCC AGG GAA GGG GGC GGA      816
      Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg Glu Gly Gly Gly
 15                   260             265             270

      GGA AAG CGC AAA GGG AAA AGC AAG AAG TGG AAA GAA ATC CTG AAG TTC      864
      Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu Ile Leu Lys Phe
                  275             280             285
 20
      CCT CAC ATT AGC CAG TGT GAA GAC CTC CGA AGG ACC ATA GAC AGA GAT      912
      Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr Ile Asp Arg Asp
          290             295             300

 25   TAC TGC AGT TTA TGT GAC AAG CAG CCA ATC GGG AGG CTG CTT TTC CGG      960
      Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg Leu Leu Phe Arg
      305             310             315             320

      CAG TTT TGT GAA ACC AGG CCT GGG CTG GAG TGT TAC ATT CAG TTC CTG     1008
 30   Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr Ile Gln Phe Leu
                  325             330             335

      GAC TCC GTG GCA GAA TAT GAA GTT ACT CCA GAT GAA AAA CTG GGA GAG     1056
      Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu Lys Leu Gly Glu
 35                   340             345             350

      AAA GGG AAG GAA ATT ATG ACC AAG TAC CTC ACC CCA AAG TCC CCT GTT     1104
      Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro Lys Ser Pro Val
                  355             360             365
 40
      TTC ATA GCC CAA GTT GGC CAA GAC CTG GTC TCC CAG ACG GAG GAG AAG     1152
      Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln Thr Glu Glu Lys
          370             375             380

 45   CTC CTA CAG AAG CCG TGC AAA GAA CTC TTT TCT GCC TGT GCA CAG TCT     1200
      Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala Cys Ala Gln Ser
      385             390             395             400

      GTC CAC GAG TAC CTG AGG GGA GAA CCA TTC CAC GAA TAT CTG GAC AGC     1248
 50   Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu Tyr Leu Asp Ser
                  405             410             415

      ATG TTT TTT GAC CGC TTT CTC CAG TGG AAG TGG TTG GAA AGG CAA CCG     1296
      Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu Glu Arg Gln Pro
 55               420             425             430
```

77

78

```
        GTG ACC AAA AAC ACT TTC AGG CAG TAT CGA GTG CTA GGA AAA GGG GGC      1344
        Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu Gly Lys Gly Gly
                435                 440                 445

  5     TTC GGG GAG GTC TGT GCC TGC CAG GTT CGG GCC ACG GGT AAA ATG TAT      1392
        Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr Gly Lys Met Tyr
                450                 455                 460

 10     GCC TGC AAG CGC TTG GAG AAG AAG AGG ATC AAA AAG AGG AAA GGG GAG      1440
        Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys Arg Lys Gly Glu
        465                 470                 475                 480

        TCC ATG GCC CTC AAT GAG AAG CAG ATC CTC GAG AAG GTC AAC AGT CAG      1488
        Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys Val Asn Ser Gln
 15                     485                 490                 495

        TTT GTG GTC AAC CTG GCC TAT GCC TAC GAG ACC AAG GAT GCA CTG TGC      1536
        Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys Asp Ala Leu Cys
                    500                 505                 510
 20
        TTG GTC CTG ACC ATC ATG AAT GGG GGT GAC CTG AAG TTC CAC ATC TAC      1584
        Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys Phe His Ile Tyr
                    515                 520                 525

 25     AAC ATG GGC AAC CCT GGC TTC GAG GAG GAG CGG GCC TTG TTT TAT GCG      1632
        Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala Leu Phe Tyr Ala
                530                 535                 540

        GCA GAG ATC CTC TGC GGC TTA GAA GAC CTC CAC CGT GAG AAC ACC GTC      1680
 30     Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg Glu Asn Thr Val
        545                 550                 555                 560

        TAC CGA GAT CTG AAA CCT GAA AAC ATC CTG TTA GAT GAT TAT GGC CAC      1728
        Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp Asp Tyr Gly His
 35                     565                 570                 575

        ATT AGG ATC TCA GAC CTG GGC TTG GCT GTG AAG ATC CCC GAG GGA GAC      1776
        Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile Pro Glu Gly Asp
                    580                 585                 590
 40
        CTG ATC CGC GGC CGG GTG GGC ACT GTT GGC TAC ATG GCC CCC GAA GTC      1824
        Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met Ala Pro Glu Val
                    595                 600                 605

 45     CTG AAC AAC CAG AGG TAC GGC CTG AGC CCC GAC TAC TGG GGC CTT GGC      1872
        Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr Trp Gly Leu Gly
                610                 615                 620

        TGC CTC ATC TAT GAG ATG ATC GAG GGC CAG TCG CCG TTC CGC GGC CGT      1920
        Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro Phe Arg Gly Arg
 50     625                 630                 635                 640

        AAG GAG AAG GTG AAG CGG GAG GAG GTG GAC CGC CGG GTC CTG GAG ACG      1968
        Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg Val Leu Glu Thr
 55                     645                 650                 655
```

78

```
GAG GAG GTG TAC TCC CAC AAG TTC TCC GAG GAG GCC AAG TCC ATC TGC      2016
Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala Lys Ser Ile Cys
            660             665                 670

AAG ATG CTG CTC ACG AAA GAT GCG AAG CAG AGG CTG GGC TGC CAG GAG      2064
Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu Gly Cys Gln Glu
            675             680                 685

GAG GGG GCT GCA GAG GTC AAG AGA CAC CCC TTC TTC AGG AAC ATG AAC      2112
Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe Arg Asn Met Asn
            690             695                 700

TTC AAG CGC TTA GAA GCC GGG ATG TTG GAC CCT CCC TTC GTT CCA GAC      2160
Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro Phe Val Pro Asp
705             710             715                 720

CCC CGC GCT GTG TAC TGT AAG GAC GTG CTG GAC ATC GAG CAG TTC TCC      2208
Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile Glu Gln Phe Ser
                725             730                 735

ACT GTG AAG GGC GTC AAT CTG GAC CAC ACA GAC GAC GAC TTC TAC TCC      2256
Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp Asp Phe Tyr Ser
            740             745                 750

AAG TTC TCC ACG GGC TCT GTG TCC ATC CCA TGG CAA AAC GAG ATG ATA      2304
Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln Asn Glu Met Ile
            755             760                 765

GAA ACA GAA TGC TTT AAG GAG CTG AAC GTG TTT GGA CCT AAT GGT ACC      2352
Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly Pro Asn Gly Thr
            770             775             780

CTC CCG CCA GAT CTG AAC AGA AAC CAC CCT CCG GAA CCG CCC AAG AAA      2400
Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu Pro Pro Lys Lys
785             790                 795                 800

GGG CTG CTC CAG AGA CTC TTC AAG CGG CAG CAT CAG AAC AAT TCC AAG      2448
Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln Asn Asn Ser Lys
                805                 810                 815

AGT TCG CCC AGC TCC AAG ACC AGT TTT AAC CAC CAC ATA AAC TCA AAC      2496
Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His Ile Asn Ser Asn
                820             825                 830

CAT GTC AGC TCG AAC TCC ACC GGA AGC AGC TAG                          2529
His Val Ser Ser Asn Ser Thr Gly Ser Ser
        835                 840
```

(2) INFORMATION FOR SEQ ID NO:43:

   (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 842 amino acids
       (B) TYPE: amino acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

```
            (ii) MOLECULE TYPE: protein
            (v) FRAGMENT TYPE: internal

  5         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

        Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
          1               5                  10                 15
        Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 10                   20                  25                 30
        Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                   35                  40                  45
        Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                   50                  55                  60
 15     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
         65                  70                  75                 80
        Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                       85                  90                  95
        Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
 20                  100                 105                 110
        Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                  115                 120                 125
        Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                  130                 135                 140
 25     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
        145                 150                 155                 160
        Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                      165                 170                 175
        Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
 30                  180                 185                 190
        Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                  195                 200                 205
        Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                  210                 215                 220
 35     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
        225                 230                 235                 240
        Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ser Met Glu Leu Glu
                      245                 250                 255
        Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg Glu Gly Gly Gly
 40                  260                 265                 270
        Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu Ile Leu Lys Phe
                  275                 280                 285
        Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr Ile Asp Arg Asp
                  290                 295                 300
 45     Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg Leu Leu Phe Arg
        305                 310                 315                 320
        Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr Ile Gln Phe Leu
                      325                 330                 335
        Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu Lys Leu Gly Glu
 50                  340                 345                 350
        Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro Lys Ser Pro Val
                      355                 360                 365
        Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln Thr Glu Glu Lys
                  370                 375                 380
 55     Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala Cys Ala Gln Ser
        385                 390                 395                 400
```

                                                                        80

```
        Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu Tyr Leu Asp Ser
                    405                 410                 415
        Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu Glu Arg Gln Pro
                    420                 425                 430
   5    Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu Gly Lys Gly Gly
                    435                 440                 445
        Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr Gly Lys Met Tyr
                    450                 455                 460
  10    Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys Arg Lys Gly Glu
        465                 470                 475                 480
        Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys Val Asn Ser Gln
                            485                 490                 495
        Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys Asp Ala Leu Cys
                    500                 505                 510
  15    Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys Phe His Ile Tyr
                    515                 520                 525
        Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala Leu Phe Tyr Ala
                    530                 535                 540
        Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg Glu Asn Thr Val
  20    545                 550                 555                 560
        Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp Asp Tyr Gly His
                            565                 570                 575
        Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile Pro Glu Gly Asp
                    580                 585                 590
  25    Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met Ala Pro Glu Val
                    595                 600                 605
        Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr Trp Gly Leu Gly
                    610                 615                 620
        Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro Phe Arg Gly Arg
  30    625                 630                 635                 640
        Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg Val Leu Glu Thr
                    645                 650                 655
        Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala Lys Ser Ile Cys
                    660                 665                 670
  35    Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu Gly Cys Gln Glu
                    675                 680                 685
        Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe Arg Asn Met Asn
                    690                 695                 700
        Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro Phe Val Pro Asp
  40    705                 710                 715                 720
        Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile Glu Gln Phe Ser
                    725                 730                 735
        Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp Asp Phe Tyr Ser
                    740                 745                 750
  45    Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln Asn Glu Met Ile
                    755                 760                 765
        Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly Pro Asn Gly Thr
                    770                 775                 780
        Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu Pro Pro Lys Lys
  50    785                 790                 795                 800
        Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln Asn Asn Ser Lys
                    805                 810                 815
        Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His Ile Asn Ser Asn
                    820                 825                 830
  55    His Val Ser Ser Asn Ser Thr Gly Ser Ser
                    835                 840
```

SUBSTITUTE SHEET (RULE 26)

(2) INFORMATION FOR SEQ ID NO:44:

    (i) SEQUENCE CHARACTERISTICS:
5
       (A) LENGTH: 1902 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

10
    (ii) MOLECULE TYPE: cDNA
    (ix) FEATURE:

       (A) NAME/KEY: Coding Sequence
       (B) LOCATION: 1...1899
15
       (D) OTHER INFORMATION:

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

```
     ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
20   Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                  10                  15

     GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
25                20                  25                  30

     GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                35                  40                  45
30
     TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                50                  55                  60

35   CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80

     CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
40   Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                        85                  90                  95

     CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
45                      100                 105                 110

     GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                115                 120                 125
50
     ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                130                 135                 140

55   AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
```

83

```
        145                    150                    155                      160
     GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
  5                      165                    170                    175

     GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
 10                      180                    185                    190

     CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                         195                    200                    205

 15  AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                         210                    215                    220

     GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
 20  Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                    230                    235                    240

     GGA CTC AGA TCT CGA GCT CGA GCC ATC ATG AGC AGA AGC AAG CGT GAC      768
     Gly Leu Arg Ser Arg Ala Arg Ala Ile Met Ser Arg Ser Lys Arg Asp
 25                      245                    250                    255

     AAC AAT TTT TAT AGT GTA GAG ATT GGA GAT TCT ACA TTC ACA GTC CTG      816
     Asn Asn Phe Tyr Ser Val Glu Ile Gly Asp Ser Thr Phe Thr Val Leu
                         260                    265                    270
 30
     AAA CGA TAT CAG AAT TTA AAA CCT ATA GGC TCA GGA GCT CAA GGA ATA      864
     Lys Arg Tyr Gln Asn Leu Lys Pro Ile Gly Ser Gly Ala Gln Gly Ile
                         275                    280                    285

 35  GTA TGC GCA GCT TAT GAT GCC ATT CTT GAA AGA AAT GTT GCA ATC AAG      912
     Val Cys Ala Ala Tyr Asp Ala Ile Leu Glu Arg Asn Val Ala Ile Lys
                         290                    295                    300

     AAG CTA AGC CGA CCA TTT CAG AAT CAG ACT CAT GCC AAG CGG GCC TAC      960
 40  Lys Leu Ser Arg Pro Phe Gln Asn Gln Thr His Ala Lys Arg Ala Tyr
     305                    310                    315                    320

     AGA GAG CTA GTT CTT ATG AAA TGT GTT AAT CAC AAA AAT ATA ATT GGC      1008
     Arg Glu Leu Val Leu Met Lys Cys Val Asn His Lys Asn Ile Ile Gly
 45                      325                    330                    335

     CTT TTG AAT GTT TTC ACA CCA CAG AAA TCC CTA GAA GAA TTT CAA GAT      1056
     Leu Leu Asn Val Phe Thr Pro Gln Lys Ser Leu Glu Glu Phe Gln Asp
                         340                    345                    350
 50
     GTT TAC ATA GTC ATG GAG CTC ATG GAT GCA AAT CTT TGC CAA GTG ATT      1104
     Val Tyr Ile Val Met Glu Leu Met Asp Ala Asn Leu Cys Gln Val Ile
                         355                    360                    365

 55  CAG ATG GAG CTA GAT CAT GAA AGA ATG TCC TAC CTT CTC TAT CAG ATG      1152
     Gln Met Glu Leu Asp His Glu Arg Met Ser Tyr Leu Leu Tyr Gln Met
```

SUBSTITUTE SHEET (RULE 26)

84

```
              370                    375                  380

     CTG TGT GGA ATC AAG CAC CTT CAT TCT GCT GGA ATT ATT CAT CGG GAC    1200
     Leu Cys Gly Ile Lys His Leu His Ser Ala Gly Ile Ile His Arg Asp
 5   385              390              395              400

     TTA AAG CCC AGT AAT ATA GTA GTA AAA TCT GAT TGC ACT TTG AAG ATT    1248
     Leu Lys Pro Ser Asn Ile Val Val Lys Ser Asp Cys Thr Leu Lys Ile
                     405              410              415
10
     CTT GAC TTC GGT CTG GCC AGG ACT GCA GGA ACG AGT TTT ATG ATG ACG    1296
     Leu Asp Phe Gly Leu Ala Arg Thr Ala Gly Thr Ser Phe Met Met Thr
                 420              425              430

15   CCT TAT GTA GTG ACT CGC TAC TAC AGA GCA CCC GAG GTC ATC CTT GGC    1344
     Pro Tyr Val Val Thr Arg Tyr Tyr Arg Ala Pro Glu Val Ile Leu Gly
                 435              440              445

     ATG GGC TAC AAG GAA AAC GTG GAT TTA TGG TCT GTG GGG TGC ATT ATG    1392
     Met Gly Tyr Lys Glu Asn Val Asp Leu Trp Ser Val Gly Cys Ile Met
20               450              455              460

     GGA GAA ATG GTT TGC CAC AAA ATC CTC TTT CCA GGA AGG GAC TAT ATT    1440
     Gly Glu Met Val Cys His Lys Ile Leu Phe Pro Gly Arg Asp Tyr Ile
25   465              470              475              480

     GAT CAG TGG AAT AAA GTT ATT GAA CAG CTT GGA ACA CCA TGT CCT GAA    1488
     Asp Gln Trp Asn Lys Val Ile Glu Gln Leu Gly Thr Pro Cys Pro Glu
                     485              490              495
30
     TTC ATG AAG AAA CTG CAA CCA ACA GTA AGG ACT TAC GTT GAA AAC AGA    1536
     Phe Met Lys Lys Leu Gln Pro Thr Val Arg Thr Tyr Val Glu Asn Arg
                     500              505              510

35   CCT AAA TAT GCT GGA TAT AGC TTT GAG AAA CTC TTC CCT GAT GTC CTT    1584
     Pro Lys Tyr Ala Gly Tyr Ser Phe Glu Lys Leu Phe Pro Asp Val Leu
                 515              520              525

     TTC CCA GCT GAC TCA GAA CAC AAC AAA CTT AAA GCC AGT CAG GCA AGG    1632
     Phe Pro Ala Asp Ser Glu His Asn Lys Leu Lys Ala Ser Gln Ala Arg
40               530              535              540

     GAT TTG TTA TCC AAA ATG CTG GTA ATA GAT GCA TCT AAA AGG ATC TCT    1680
     Asp Leu Leu Ser Lys Met Leu Val Ile Asp Ala Ser Lys Arg Ile Ser
45   545              550              555              560

     GTA GAT GAA GCT CTC CAA CAC CCG TAC ATC AAT GTC TGG TAT GAT CCT    1728
     Val Asp Glu Ala Leu Gln His Pro Tyr Ile Asn Val Trp Tyr Asp Pro
                 565              570              575
50
     TCT GAA GCA GAA GCT CCA CCA CCA AAG ATC CCT GAC AAG CAG TTA GAT    1776
     Ser Glu Ala Glu Ala Pro Pro Pro Lys Ile Pro Asp Lys Gln Leu Asp
                     580              585              590

55   GAA AGG GAA CAC ACA ATA GAA GAG TGG AAA GAA TTG ATA TAT AAG GAA    1824
     Glu Arg Glu His Thr Ile Glu Glu Trp Lys Glu Leu Ile Tyr Lys Glu
```

84

SUBSTITUTE SHEET (RULE 26)

85

```
           595                    600                    605
      GTT ATG GAC TTG GAG GAG AGA ACC AAG AAT GGA GTT ATA CGG GGG CAG    1872
      Val Met Asp Leu Glu Glu Arg Thr Lys Asn Gly Val Ile Arg Gly Gln
 5        610                    615                    620

      CCC TCT CCT TTA GCA CAG GTG CAG CAG TGA                           1902
      Pro Ser Pro Leu Ala Gln Val Gln Gln
      625                    630
10
```

(2) INFORMATION FOR SEQ ID NO:45:

    (i) SEQUENCE CHARACTERISTICS:
15   (A) LENGTH: 633 amino acids
        (B) TYPE: amino acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

20   (ii) MOLECULE TYPE: protein
        (v) FRAGMENT TYPE: internal

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

```
25   Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
     1                   5                   10                  15
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                    20                  25                  30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
30                  35                  40                  45
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                    50                  55                  60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80
35   Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                    85                  90                  95
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100                 105                 110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
40                  115                 120                 125
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                    130                 135                 140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160
45   Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                    165                 170                 175
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                    180                 185                 190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
50                  195                 200                 205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                    210                 215                 220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240
55   Gly Leu Arg Ser Arg Ala Arg Ala Ile Met Ser Arg Ser Lys Arg Asp
                    245                 250                 255
```

BNSDOCID: <WO___9845704A2_I_>

```
     Asn Asn Phe Tyr Ser Val Glu Ile Gly Asp Ser Thr Phe Thr Val Leu
                 260                     265                 270
     Lys Arg Tyr Gln Asn Leu Lys Pro Ile Gly Ser Gly Ala Gln Gly Ile
                 275                     280                 285
5    Val Cys Ala Ala Tyr Asp Ala Ile Leu Glu Arg Asn Val Ala Ile Lys
             290                     295                 300
     Lys Leu Ser Arg Pro Phe Gln Asn Gln Thr His Ala Lys Arg Ala Tyr
     305                     310                 315                 320
     Arg Glu Leu Val Leu Met Lys Cys Val Asn His Lys Asn Ile Ile Gly
10                           325                 330                 335
     Leu Leu Asn Val Phe Thr Pro Gln Lys Ser Leu Glu Glu Phe Gln Asp
                 340                     345                 350
     Val Tyr Ile Val Met Glu Leu Met Asp Ala Asn Leu Cys Gln Val Ile
                 355                     360                 365
15   Gln Met Glu Leu Asp His Glu Arg Met Ser Tyr Leu Leu Tyr Gln Met
             370                     375                 380
     Leu Cys Gly Ile Lys His Leu His Ser Ala Gly Ile Ile His Arg Asp
     385                     390                 395                 400
     Leu Lys Pro Ser Asn Ile Val Val Lys Ser Asp Cys Thr Leu Lys Ile
20                           405                 410                 415
     Leu Asp Phe Gly Leu Ala Arg Thr Ala Gly Thr Ser Phe Met Met Thr
                 420                     425                 430
     Pro Tyr Val Val Thr Arg Tyr Tyr Arg Ala Pro Glu Val Ile Leu Gly
                 435                     440                 445
25   Met Gly Tyr Lys Glu Asn Val Asp Leu Trp Ser Val Gly Cys Ile Met
             450                     455                 460
     Gly Glu Met Val Cys His Lys Ile Leu Phe Pro Gly Arg Asp Tyr Ile
     465                     470                 475                 480
     Asp Gln Trp Asn Lys Val Ile Glu Gln Leu Gly Thr Pro Cys Pro Glu
30                           485                 490                 495
     Phe Met Lys Lys Leu Gln Pro Thr Val Arg Thr Tyr Val Glu Asn Arg
                 500                     505                 510
     Pro Lys Tyr Ala Gly Tyr Ser Phe Glu Lys Leu Phe Pro Asp Val Leu
                 515                     520                 525
35   Phe Pro Ala Asp Ser Glu His Asn Lys Leu Lys Ala Ser Gln Ala Arg
             530                     535                 540
     Asp Leu Leu Ser Lys Met Leu Val Ile Asp Ala Ser Lys Arg Ile Ser
     545                     550                 555                 560
     Val Asp Glu Ala Leu Gln His Pro Tyr Ile Asn Val Trp Tyr Asp Pro
40                           565                 570                 575
     Ser Glu Ala Glu Ala Pro Pro Pro Lys Ile Pro Asp Lys Gln Leu Asp
                 580                     585                 590
     Glu Arg Glu His Thr Ile Glu Glu Trp Lys Glu Leu Ile Tyr Lys Glu
                 595                     600                 605
45   Val Met Asp Leu Glu Glu Arg Thr Lys Asn Gly Val Ile Arg Gly Gln
             610                     615                 620
     Pro Ser Pro Leu Ala Gln Val Gln Gln
     625                     630
```

50   (2) INFORMATION FOR SEQ ID NO:46:

            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 1824 base pairs
                (B) TYPE: nucleic acid
55   (C) STRANDEDNESS: single
                (D) TOPOLOGY: linear

```
        (ii) MOLECULE TYPE: cDNA
        (ix) FEATURE:

5               (A) NAME/KEY: Coding Sequence
                (B) LOCATION: 1...1821
                (D) OTHER INFORMATION:

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:
10
    ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG        48
    Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
     1               5                   10                  15

15  GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC        96
    Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                    20                  25                  30

    GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC       144
20  Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                35                  40                  45

    TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC       192
    Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
25      50                  55                  60

    CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG       240
    Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
    65                  70                  75                  80
30
    CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG       288
    Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                    85                  90                  95

35  CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG       336
    Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100                 105                 110

    GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC       384
40  Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                115                 120                 125

    ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC       432
    Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
45      130                 135                 140

    AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC       480
    Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
    145                 150                 155                 160
50
    GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC       528
    Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                    165                 170                 175

55  GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC       576
    Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
```

87

88

```
              180                  185                  190

      CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
  5           195                  200                  205

      AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
      Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
              210                  215                  220
 10

      GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
      Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
      225                  230                  235                  240

 15   GGA CTC AGA TCT CGA GGG AAA ATG TCT CAG GAG AGG CCC ACG TTC TAC    768
      Gly Leu Arg Ser Arg Gly Lys Met Ser Gln Glu Arg Pro Thr Phe Tyr
                       245                  250                  255

      CGG CAG GAG CTG AAC AAG ACA ATC TGG GAG GTG CCC GAG CGT TAC CAG    816
      Arg Gln Glu Leu Asn Lys Thr Ile Trp Glu Val Pro Glu Arg Tyr Gln
 20                    260                  265                  270

      AAC CTG TCT CCA GTG GGC TCT GGC GCC TAT GGC TCT GTG TGT GCT GCT    864
      Asn Leu Ser Pro Val Gly Ser Gly Ala Tyr Gly Ser Val Cys Ala Ala
 25               275                  280                  285

      TTT GAC ACA AAA ACG GGG TTA CGT GTG GCA GTG AAG AAG CTC TCC AGA    912
      Phe Asp Thr Lys Thr Gly Leu Arg Val Ala Val Lys Lys Leu Ser Arg
              290                  295                  300
 30

      CCA TTT CAG TCC ATC ATT CAT GCG AAA AGA ACC TAC AGA GAA CTG CGG    960
      Pro Phe Gln Ser Ile Ile His Ala Lys Arg Thr Tyr Arg Glu Leu Arg
      305                  310                  315                  320

 35   TTA CTT AAA CAT ATG AAA CAT GAA AAT GTG ATT GGT CTG TTG GAC GTT   1008
      Leu Leu Lys His Met Lys His Glu Asn Val Ile Gly Leu Leu Asp Val
                       325                  330                  335

      TTT ACA CCT GCA AGG TCT CTG GAG GAA TTC AAT GAT GTG TAT CTG GTG   1056
      Phe Thr Pro Ala Arg Ser Leu Glu Glu Phe Asn Asp Val Tyr Leu Val
 40               340                  345                  350

      ACC CAT CTC ATG GGG GCA GAT CTG AAC AAC ATT GTG AAA TGT CAG AAG   1104
      Thr His Leu Met Gly Ala Asp Leu Asn Asn Ile Val Lys Cys Gln Lys
 45               355                  360                  365

      CTT ACA GAT GAC CAT GTT CAG TTC CTT ATC TAC CAA ATT CTC CGA GGT   1152
      Leu Thr Asp Asp His Val Gln Phe Leu Ile Tyr Gln Ile Leu Arg Gly
              370                  375                  380
 50

      CTA AAG TAT ATA CAT TCA GCT GAC ATA ATT CAC AGG GAC CTA AAA CCT   1200
      Leu Lys Tyr Ile His Ser Ala Asp Ile Ile His Arg Asp Leu Lys Pro
      385                  390                  395                  400

 55   AGT AAT CTA GCT GTG AAT GAA GAC TGT GAG CTG AAG ATT CTG GAT TTT   1248
      Ser Asn Leu Ala Val Asn Glu Asp Cys Glu Leu Lys Ile Leu Asp Phe
```

88

SUBSTITUTE SHEET (RULE 26)

89

```
                          405                        410                          415

      GGA CTG GCT CGG CAC ACA GAT GAT GAA ATG ACA GGC TAC GTG GCC ACT     1296
 5    Gly Leu Ala Arg His Thr Asp Asp Glu Met Thr Gly Tyr Val Ala Thr
                      420                    425                    430

      AGG TGG TAC AGG GCT CCT GAG ATC ATG CTG AAC TGG ATG CAT TAC AAC     1344
      Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Trp Met His Tyr Asn
                      435                    440                    445
10
      CAG ACA GTT GAT ATT TGG TCA GTG GGA TGC ATA ATG GCC GAG CTG TTG     1392
      Gln Thr Val Asp Ile Trp Ser Val Gly Cys Ile Met Ala Glu Leu Leu
                      450                    455                    460

15    ACT GGA AGA ACA TTG TTT CCT GGT ACA GAC CAT ATT GAT CAG TTG AAG     1440
      Thr Gly Arg Thr Leu Phe Pro Gly Thr Asp His Ile Asp Gln Leu Lys
      465                    470                    475                    480

      CTC ATT TTA AGA CTC GTT GGA ACC CCA GGG GCT GAG CTT TTG AAG AAA     1488
20    Leu Ile Leu Arg Leu Val Gly Thr Pro Gly Ala Glu Leu Leu Lys Lys
                          485                    490                    495

      ATC TCC TCA GAG TCT GCA AGA AAC TAT ATT CAG TCT TTG ACT CAG ATG     1536
      Ile Ser Ser Glu Ser Ala Arg Asn Tyr Ile Gln Ser Leu Thr Gln Met
25                        500                    505                    510

      CCG AAG ATG AAC TTT GCG AAT GTA TTT ATT GGT GCC AAT CCC CTG GCT     1584
      Pro Lys Met Asn Phe Ala Asn Val Phe Ile Gly Ala Asn Pro Leu Ala
                      515                    520                    525
30
      GTC GAC TTG CTG GAG AAG ATG CTT GTA TTG GAC TCA GAT AAG AGA ATT     1632
      Val Asp Leu Leu Glu Lys Met Leu Val Leu Asp Ser Asp Lys Arg Ile
                      530                    535                    540

35    ACA GCG GCC CAA GCC CTT GCA CAT GCC TAC TTT GCT CAG TAC CAC GAT     1680
      Thr Ala Ala Gln Ala Leu Ala His Ala Tyr Phe Ala Gln Tyr His Asp
      545                    550                    555                    560

      CCT GAT GAT GAA CCA GTG GCC GAT CCT TAT GAT CAG TCC TTT GAA AGC     1728
40    Pro Asp Asp Glu Pro Val Ala Asp Pro Tyr Asp Gln Ser Phe Glu Ser
                          565                    570                    575

      AGG GAC CTC CTT ATA GAT GAG TGG AAA AGC CTG ACC TAT GAT GAA GTC     1776
      Arg Asp Leu Leu Ile Asp Glu Trp Lys Ser Leu Thr Tyr Asp Glu Val
45                    580                    585                    590

      ATC AGC TTT GTG CCA CCA CCC CTT GAC CAA GAA GAG ATG GAG TCC TGA     1824
      Ile Ser Phe Val Pro Pro Pro Leu Asp Gln Glu Glu Met Glu Ser
                      595                    600                    605
50
```

          (2) INFORMATION FOR SEQ ID NO:47:

          (i) SEQUENCE CHARACTERISTICS:
55   (A) LENGTH: 607 amino acids
               (B) TYPE: amino acid

SUBSTITUTE SHEET (RULE 26)

90

```
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein
 5      (v) FRAGMENT TYPE: internal

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
10    1               5                  10                 15
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                20                 25                 30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                35                 40                 45
15   Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                50                 55                 60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                 70                 75                 80
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
20              85                 90                 95
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                100                105                110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                115                120                125
25   Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                130                135                140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                150                155                160
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
30              165                170                175
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                180                185                190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                195                200                205
35   Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                210                215                220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                230                235                240
     Gly Leu Arg Ser Arg Gly Lys Met Ser Gln Glu Arg Pro Thr Phe Tyr
40              245                250                255
     Arg Gln Glu Leu Asn Lys Thr Ile Trp Glu Val Pro Glu Arg Tyr Gln
                260                265                270
     Asn Leu Ser Pro Val Gly Ser Gly Ala Tyr Gly Ser Val Cys Ala Ala
                275                280                285
45   Phe Asp Thr Lys Thr Gly Leu Arg Val Ala Val Lys Lys Leu Ser Arg
                290                295                300
     Pro Phe Gln Ser Ile Ile His Ala Lys Arg Thr Tyr Arg Glu Leu Arg
     305                310                315                320
     Leu Leu Lys His Met Lys His Glu Asn Val Ile Gly Leu Leu Asp Val
50              325                330                335
     Phe Thr Pro Ala Arg Ser Leu Glu Glu Phe Asn Asp Val Tyr Leu Val
                340                345                350
     Thr His Leu Met Gly Ala Asp Leu Asn Asn Ile Val Lys Cys Gln Lys
                355                360                365
55   Leu Thr Asp Asp His Val Gln Phe Leu Ile Tyr Gln Ile Leu Arg Gly
                370                375                380
```

91

```
     Leu Lys Tyr Ile His Ser Ala Asp Ile Ile His Arg Asp Leu Lys Pro
     385                 390                 395                 400
     Ser Asn Leu Ala Val Asn Glu Asp Cys Glu Leu Lys Ile Leu Asp Phe
                     405                 410                 415
 5   Gly Leu Ala Arg His Thr Asp Asp Glu Met Thr Gly Tyr Val Ala Thr
                     420                 425                 430
     Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Trp Met His Tyr Asn
                 435                 440                 445
     Gln Thr Val Asp Ile Trp Ser Val Gly Cys Ile Met Ala Glu Leu Leu
10       450                 455                 460
     Thr Gly Arg Thr Leu Phe Pro Gly Thr Asp His Ile Asp Gln Leu Lys
     465                 470                 475                 480
     Leu Ile Leu Arg Leu Val Gly Thr Pro Gly Ala Glu Leu Leu Lys Lys
                     485                 490                 495
15   Ile Ser Ser Glu Ser Ala Arg Asn Tyr Ile Gln Ser Leu Thr Gln Met
                 500                 505                 510
     Pro Lys Met Asn Phe Ala Asn Val Phe Ile Gly Ala Asn Pro Leu Ala
                 515                 520                 525
     Val Asp Leu Leu Glu Lys Met Leu Val Leu Asp Ser Asp Lys Arg Ile
20       530                 535                 540
     Thr Ala Ala Gln Ala Leu Ala His Ala Tyr Phe Ala Gln Tyr His Asp
     545                 550                 555                 560
     Pro Asp Asp Glu Pro Val Ala Asp Pro Tyr Asp Gln Ser Phe Glu Ser
                     565                 570                 575
25   Arg Asp Leu Leu Ile Asp Glu Trp Lys Ser Leu Thr Tyr Asp Glu Val
                 580                 585                 590
     Ile Ser Phe Val Pro Pro Pro Leu Asp Gln Glu Glu Met Glu Ser
                 595                 600                 605
```

30   (2) INFORMATION FOR SEQ ID NO:48:

           (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 2907 base pairs
               (B) TYPE: nucleic acid
35   (C) STRANDEDNESS: single
               (D) TOPOLOGY: linear

           (ii) MOLECULE TYPE: cDNA
           (ix) FEATURE:
40
               (A) NAME/KEY: Coding Sequence
               (B) LOCATION: 1...2904
               (D) OTHER INFORMATION:

45   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

```
     ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
     1               5                   10                  15
50
     GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                     20                  25                  30

55   GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
```

91

SUBSTITUTE SHEET (RULE 26)

92

```
             35                      40                      45

      TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC        192
      Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 5        50                  55                  60

      CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG        240
      Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
      65                  70                  75                  80
10

      CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG        288
      Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                      85                  90                  95

15    CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG        336
      Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                      100                 105                 110

      GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC        384
20    Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                      115                 120                 125

      ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC        432
      Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
25        130                 135                 140

      AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC        480
      Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
      145                 150                 155                 160
30
      GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC        528
      Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                      165                 170                 175

35    GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC        576
      Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                      180                 185                 190

      CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG        624
40    Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                      195                 200                 205

      AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC        672
      Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
45        210                 215                 220

      GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC        720
      Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
      225                 230                 235                 240
50
      GGA CTC AGA TCT ATG AGT GCT GAG GGG TAC CAG TAC AGA GCG CTG TAT        768
      Gly Leu Arg Ser Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr
                      245                 250                 255

55    GAT TAT AAA AAG GAA AGA GAA GAA GAT ATT GAC TTG CAC TTG GGT GAC        816
      Asp Tyr Lys Lys Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp
```

SUBSTITUTE SHEET (RULE 26)

93

<pre>
                 260   265   270

     ATA TTG ACT GTG AAT AAA GGG TCC TTA GTA GCT CTT GGA TTC AGT GAT   864
     Ile Leu Thr Val Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp
 5   275   280   285

     GGA CAG GAA GCC AGG CCT GAA GAA ATT GGC TGG TTA AAT GGC TAT AAT   912
     Gly Gln Glu Ala Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn
             290   295   300
10
     GAA ACC ACA GGG GAA AGG GGG GAC TTT CCG GGA ACT TAC GTA GAA TAT   960
     Glu Thr Thr Gly Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr
     305   310   315   320

15   ATT GGA AGG AAA AAA ATC TCG CCT CCC ACA CCA AAG CCC CGG CCA CCT   1008
     Ile Gly Arg Lys Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro
                     325   330   335

     CGG CCT CTT CCT GTT GCA CCA GGT TCT TCG AAA ACT GAA GCA GAT GTT   1056
20   Arg Pro Leu Pro Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val
                         340   345   350

     GAA CAA CAA GCT TTG ACT CTC CCG GAT CTT GCA GAG CAG TTT GCC CCT   1104
     Glu Gln Gln Ala Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro
25   355   360   365

     CCT GAC ATT GCC CCG CCT CTT CTT ATC AAG CTC GTG GAA GCC ATT GAA   1152
     Pro Asp Ile Ala Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu
             370   375   380
30
     AAG AAA GGT CTG GAA TGT TCA ACT CTA TAC AGA ACA CAG AGC TCC AGC   1200
     Lys Lys Gly Leu Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser
     385   390   395   400

35   AAC CTG GCA GAA TTA CGA CAG CTT CTT GAT TGT GAT ACA CCC TCC GTG   1248
     Asn Leu Ala Glu Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val
                     405   410   415

     GAC TTG GAA ATG ATC GAT GTG CAC GTT TTG GCT GAC GCT TTC AAA CGC   1296
40   Asp Leu Glu Met Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg
                         420   425   430

     TAT CTC CTG GAC TTA CCA AAT CCT GTC ATT CCA GCA GCC GTT TAC AGT   1344
     Tyr Leu Leu Asp Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser
45   435   440   445

     GAA ATG ATT TCT TTA GCT CCA GAA GTA CAA AGC TCC GAA GAA TAT ATT   1392
     Glu Met Ile Ser Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile
             450   455   460
50
     CAG CTA TTG AAG AAG CTT ATT AGG TCG CCT AGC ATA CCT CAT CAG TAT   1440
     Gln Leu Leu Lys Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr
     465   470   475   480

55   TGG CTT ACG CTT CAG TAT TTG TTA AAA CAT TTC TTC AAG CTC TCT CAA   1488
     Trp Leu Thr Leu Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln
</pre>

93

94

```
                    485                      490                      495

      ACC TCC AGC AAA AAT CTG TTG AAT GCA AGA GTA CTC TCT GAA ATT TTC      1536
      Thr Ser Ser Lys Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe
 5            500                      505                      510

      AGC CCT ATG CTT TTC AGA TTC TCA GCA GCC AGC TCT GAT AAT ACT GAA      1584
      Ser Pro Met Leu Phe Arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu
              515                      520                      525
10

      AAC CTC ATA AAA GTT ATA GAA ATT TTA ATC TCA ACT GAA TGG AAT GAA      1632
      Asn Leu Ile Lys Val Ile Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu
              530                      535                      540

15    CGA CAG CCT GCA CCA GCA CTG CCT CCT AAA CCA CCA AAA CCT ACT ACT      1680
      Arg Gln Pro Ala Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr
      545                      550                      555                      560

      GTA GCC AAC AAC GGT ATG AAT AAC AAT ATG TCC TTA CAA AAT GCT GAA      1728
20    Val Ala Asn Asn Gly Met Asn Asn Asn Met Ser Leu Gln Asn Ala Glu
                          565                      570                      575

      TGG TAC TGG GGA GAT ATC TCG AGG GAA GAA GTG AAT GAA AAA CTT CGA      1776
      Trp Tyr Trp Gly Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg
25                        580                      585                      590

      GAT ACA GCA GAC GGG ACC TTT TTG GTA CGA GAT GCG TCT ACT AAA ATG      1824
      Asp Thr Ala Asp Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met
              595                      600                      605
30

      CAT GGT GAT TAT ACT CTT ACA CTA AGG AAA GGG GGA AAT AAC AAA TTA      1872
      His Gly Asp Tyr Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu
              610                      615                      620

35    ATC AAA ATA TTT CAT CGA GAT GGG AAA TAT GGC TTC TCT GAC CCA TTA      1920
      Ile Lys Ile Phe His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu
      625                      630                      635                      640

      ACC TTC AGT TCT GTG GTT GAA TTA ATA AAC CAC TAC CGG AAT GAA TCT      1968
40    Thr Phe Ser Ser Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser
                          645                      650                      655

      CTA GCT CAG TAT AAT CCC AAA TTG GAT GTG AAA TTA CTT TAT CCA GTA      2016
      Leu Ala Gln Tyr Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val
45                        660                      665                      670

      TCC AAA TAC CAA CAG GAT CAA GTT GTC AAA GAA GAT AAT ATT GAA GCT      2064
      Ser Lys Tyr Gln Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala
              675                      680                      685
50

      GTA GGG AAA AAA TTA CAT GAA TAT AAC ACT CAG TTT CAA GAA AAA AGT      2112
      Val Gly Lys Lys Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser
              690                      695                      700

55    CGA GAA TAT GAT AGA TTA TAT GAA GAA TAT ACC CGC ACA TCC CAG GAA      2160
      Arg Glu Tyr Asp Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu
```

94

SUBSTITUTE SHEET (RULE 26)

```
           705                      710                     715                    720

       ATC CAA ATG AAA AGG ACA GCT ATT GAA GCA TTT AAT GAA ACC ATA AAA      2208
       Ile Gln Met Lys Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys
  5                     725                     730                     735

       ATA TTT GAA GAA CAG TGC CAG ACC CAA GAG CGG TAC AGC AAA GAA TAC      2256
       Ile Phe Glu Glu Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr
                        740                     745                     750
 10
       ATA GAA AAG TTT AAA CGT GAA GGC AAT GAG AAA GAA ATA CAA AGG ATT      2304
       Ile Glu Lys Phe Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile
                    755                     760                     765
 15
       ATG CAT AAT TAT GAT AAG TTG AAG TCT CGA ATC AGT GAA ATT ATT GAC      2352
       Met His Asn Tyr Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp
                    770                     775                     780

       AGT AGA AGA AGA TTG GAA GAA GAC TTG AAG AAG CAG GCA GCT GAG TAT      2400
 20    Ser Arg Arg Arg Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr
       785                     790                     795                     800

       CGA GAA ATT GAC AAA CGT ATG AAC AGC ATT AAA CCA GAC CTT ATC CAG      2448
       Arg Glu Ile Asp Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln
 25                     805                     810                     815

       CTG AGA AAG ACG AGA GAC CAA TAC TTG ATG TGG TTG ACT CAA AAA GGT      2496
       Leu Arg Lys Thr Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly
                        820                     825                     830
 30
       GTT CGG CAA AAG AAG TTG AAC GAG TGG TTG GGC AAT GAA AAC ACT GAA      2544
       Val Arg Gln Lys Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu
                        835                     840                     845

 35    GAC CAA TAT TCA CTG GTG GAA GAT GAT GAA GAT TTG CCC CAT CAT GAT      2592
       Asp Gln Tyr Ser Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp
                    850                     855                     860

       GAG AAG ACA TGG AAT GTT GGA AGC AGC AAC CGA AAC AAA GCT GAA AAC      2640
 40    Glu Lys Thr Trp Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn
       865                     870                     875                     880

       CTG TTG CGA GGG AAG CGA GAT GGC ACT TTT CTT GTC CGG GAG AGC AGT      2688
       Leu Leu Arg Gly Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser
 45                     885                     890                     895

       AAA CAG GGC TGC TAT GCC TGC TCT GTA GTG GTG GAC GGC GAA GTA AAG      2736
       Lys Gln Gly Cys Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys
                        900                     905                     910
 50
 -     CAT TGT GTC ATA AAC AAA ACA GCA ACT GGC TAT GGC TTT GCC GAG CCC      2784
       His Cys Val Ile Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro
                    915                     920                     925

 55    TAT AAC TTG TAC AGC TCT CTG AAA GAA CTG GTG CTA CAT TAC CAA CAC      2832
       Tyr Asn Leu Tyr Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His
```

96

```
        930                     935                     940
      ACC TCC CTT GTG CAG CAC AAC GAC TCC CTC AAT GTC ACA CTA GCC TAC        2880
      Thr Ser Leu Val Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr
  5   945                     950                     955                 960

      CCA GTA TAT GCA CAG CAG AGG CGA TGA                                     2907
      Pro Val Tyr Ala Gln Gln Arg Arg
                          965
 10
```

            (2) INFORMATION FOR SEQ ID NO:49:

            (i) SEQUENCE CHARACTERISTICS:
 15   (A) LENGTH: 968 amino acids
                 (B) TYPE: amino acid
                 (C) STRANDEDNESS: single
                 (D) TOPOLOGY: linear

 20   (ii) MOLECULE TYPE: protein
            (v) FRAGMENT TYPE: internal

            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

```
 25   Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
       1               5              10                  15
      Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                  20                  25                  30
      Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 30               35                  40                  45
      Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                  50                  55                  60
      Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
      65                  70                  75                  80
 35   Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                      85                  90                  95
      Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                  100                 105                 110
      Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 40               115                 120                 125
      Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                  130                 135                 140
      Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
      145                 150                 155                 160
 45   Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                      165                 170                 175
      Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                  180                 185                 190
      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
 50               195                 200                 205
      Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                  210                 215                 220
      Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
      225                 230                 235                 240
 55   Gly Leu Arg Ser Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr
                      245                 250                 255
```

                                                                        96

SUBSTITUTE SHEET (RULE 26)

97

```
       Asp Tyr Lys Lys Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp
                   260                 265                 270
       Ile Leu Thr Val Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp
                   275                 280                 285
  5    Gly Gln Glu Ala Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn
                   290                 295                 300
       Glu Thr Thr Gly Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr
       305                 310                 315                 320
       Ile Gly Arg Lys Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro
  10                   325                 330                 335
       Arg Pro Leu Pro Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val
                   340                 345                 350
       Glu Gln Gln Ala Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro
                   355                 360                 365
  15   Pro Asp Ile Ala Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu
                   370                 375                 380
       Lys Lys Gly Leu Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser
       385                 390                 395                 400
       Asn Leu Ala Glu Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val
  20                   405                 410                 415
       Asp Leu Glu Met Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg
                   420                 425                 430
       Tyr Leu Leu Asp Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser
                   435                 440                 445
  25   Glu Met Ile Ser Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile
                   450                 455                 460
       Gln Leu Leu Lys Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr
       465                 470                 475                 480
       Trp Leu Thr Leu Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln
  30                   485                 490                 495
       Thr Ser Ser Lys Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe
                   500                 505                 510
       Ser Pro Met Leu Phe Arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu
                   515                 520                 525
  35   Asn Leu Ile Lys Val Ile Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu
                   530                 535                 540
       Arg Gln Pro Ala Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr
       545                 550                 555                 560
       Val Ala Asn Asn Gly Met Asn Asn Asn Met Ser Leu Gln Asn Ala Glu
  40                   565                 570                 575
       Trp Tyr Trp Gly Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg
                   580                 585                 590
       Asp Thr Ala Asp Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met
                   595                 600                 605
  45   His Gly Asp Tyr Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu
                   610                 615                 620
       Ile Lys Ile Phe His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu
       625                 630                 635                 640
       Thr Phe Ser Ser Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser
  50                   645                 650                 655
       Leu Ala Gln Tyr Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val
                   660                 665                 670
       Ser Lys Tyr Gln Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala
                   675                 680                 685
  55   Val Gly Lys Lys Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser
                   690                 695                 700
```

```
Arg Glu Tyr Asp Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu
705                 710                 715                 720
Ile Gln Met Lys Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys
            725                 730                 735
Ile Phe Glu Glu Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr
            740                 745                 750
Ile Glu Lys Phe Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile
        755                 760                 765
Met His Asn Tyr Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp
    770                 775                 780
Ser Arg Arg Arg Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr
785                 790                 795                 800
Arg Glu Ile Asp Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln
            805                 810                 815
Leu Arg Lys Thr Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly
        820                 825                 830
Val Arg Gln Lys Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu
        835                 840                 845
Asp Gln Tyr Ser Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp
    850                 855                 860
Glu Lys Thr Trp Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn
865                 870                 875                 880
Leu Leu Arg Gly Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser
            885                 890                 895
Lys Gln Gly Cys Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys
            900                 905                 910
His Cys Val Ile Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro
    915                 920                 925
Tyr Asn Leu Tyr Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His
    930                 935                 940
Thr Ser Leu Val Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr
945                 950                 955                 960
Pro Val Tyr Ala Gln Gln Arg Arg
            965
```

        (2) INFORMATION FOR SEQ ID NO:50:

        (i) SEQUENCE CHARACTERISTICS:
           (A) LENGTH: 2160 base pairs
           (B) TYPE: nucleic acid
           (C) STRANDEDNESS: single
           (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: cDNA
        (ix) FEATURE:

           (A) NAME/KEY: Coding Sequence
           (B) LOCATION: 1...2157
           (D) OTHER INFORMATION:

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
  1               5                   10                  15
```

99

```
      GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC       96
      Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                  20              25              30

 5    GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC      144
      Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                  35              40              45

10    TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC      192
      Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                  50              55              60

      CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG      240
      Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
15    65                  70              75                  80

      CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG      288
      Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                      85                  90                  95

20    CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG      336
      Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                      100             105             110

25    GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC      384
      Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                  115                 120             125

      ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC      432
30    Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                  130             135                 140

      AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC      480
      Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
35    145                 150                 155                 160

      GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
      Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                      165                 170                 175
40
      GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
      Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                  180                 185                 190

45    CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                  195                 200                 205

      AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
50    Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                  210                 215                 220

      GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
      Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
55    225                 230                 235                 240
```

SUBSTITUTE SHEET (RULE 26)

100

```
        GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG ACC ATG TCG TCC ATC        768
        Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ser Ser Ile
                        245             250                 255

 5      TTG CCA TTC ACG CCG CCA GTT GTG AAG AGA CTG CTG GGA TGG AAG AAG        816
        Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu Gly Trp Lys Lys
                        260             265                 270

10      TCA GCT GGT GGG TCT GGA GGA GCA GGC GGA GGA GAG CAG AAT GGG CAG        864
        Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu Gln Asn Gly Gln
                        275             280                 285

        GAA GAA AAG TGG TGT GAG AAA GCA GTG AAA AGT CTG GTG AAG AAG CTA        912
        Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu Val Lys Lys Leu
15                      290             295                 300

        AAG AAA ACA GGA CGA TTA GAT GAG CTT GAG AAA GCC ATC ACC ACT CAA        960
        Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala Ile Thr Thr Gln
        305                 310                 315                 320
20
        AAC TGT AAT ACT AAA TGT GTT ACC ATA CCA AGC ACT TGC TCT GAA ATT        1008
        Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr Cys Ser Glu Ile
                        325                 330                 335

25      TGG GGA CTG AGT ACA CCA AAT ACG ATA GAT CAG TGG GAT ACA ACA GGC        1056
        Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp Asp Thr Thr Gly
                        340                 345                 350

        CTT TAC AGC TTC TCT GAA CAA ACC AGG TCT CTT GAT GGT CGT CTC CAG        1104
30      Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp Gly Arg Leu Gln
                        355                 360                 365

        GTA TCC CAT CGA AAA GGA TTG CCA CAT GTT ATA TAT TGC CGA TTA TGG        1152
        Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr Cys Arg Leu Trp
35                      370                 375                 380

        CGC TGG CCT GAT CTT CAC AGT CAT CAT GAA CTC AAG GCA ATT GAA AAC        1200
        Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys Ala Ile Glu Asn
        385                 390                 395                 400
40
        TGC GAA TAT GCT TTT AAT CTT AAA AAG GAT GAA GTA TGT GTA AAC CCT        1248
        Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val Cys Val Asn Pro
                        405                 410                 415

45      TAC CAC TAT CAG AGA GTT GAG ACA CCA GTT TTG CCT CCA GTA TTA GTG        1296
        Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro Pro Val Leu Val
                        420                 425                 430

        CCC CGA CAC ACC GAG ATC CTA ACA GAA CTT CCG CCT CTG GAT GAC TAT        1344
50      Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro Leu Asp Asp Tyr
                        435                 440                 445

        ACT CAC TCC ATT CCA GAA AAC ACT AAC TTC CCA GCA GGA ATT GAG CCA        1392
        Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala Gly Ile Glu Pro
55                      450                 455                 460
```

BNSDOCID: <WO___9845704A2_I_>

101

```
     CAG AGT AAT TAT ATT CCA GAA ACG CCA CCT CCT GGA TAT ATC AGT GAA        1440
     Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly Tyr Ile Ser Glu
     465              470              475              480

 5   GAT GGA GAA ACA AGT GAC CAA CAG TTG AAT CAA AGT ATG GAC ACA GGC        1488
     Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser Met Asp Thr Gly
                     485              490              495

     TCT CCA GCA GAA CTA TCT CCT ACT ACT CTT TCC CCT GTT AAT CAT AGC        1536
10   Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro Val Asn His Ser
                     500              505              510

     TTG GAT TTA CAG CCA GTT ACT TAC TCA GAA CCT GCA TTT TGG TGT TCA        1584
     Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala Phe Trp Cys Ser
15                   515              520              525

     ATA GCA TAT TAT GAA TTA AAT CAG AGG GTT GGA GAA ACC TTC CAT GCA        1632
     Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu Thr Phe His Ala
                     530              535              540
20
     TCA CAG CCC TCA CTC ACT GTA GAT GGC TTT ACA GAC CCA TCA AAT TCA        1680
     Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp Pro Ser Asn Ser
     545              550              555              560

25   GAG AGG TTC TGC TTA GGT TTA CTC TCC AAT GTT AAC CGA AAT GCC ACG        1728
     Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn Arg Asn Ala Thr
                     565              570              575

     GTA GAA ATG ACA AGA AGG CAT ATA GGA AGA GGA GTG CGC TTA TAC TAC        1776
30   Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val Arg Leu Tyr Tyr
                     580              585              590

     ATA GGT GGG GAA GTT TTT GCT GAG TGC CTA AGT GAT AGT GCA ATC TTT        1824
     Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp Ser Ala Ile Phe
35                   595              600              605

     GTG CAG AGC CCC AAT TGT AAT CAG AGA TAT GGC TGG CAC CCT GCA ACA        1872
     Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp His Pro Ala Thr
                     610              615              620
40
     GTG TGT AAA ATT CCA CCA GGC TGT AAT CTG AAG ATC TTC AAC AAC CAG        1920
     Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile Phe Asn Asn Gln
     625              630              635              640

45   GAA TTT GCT GCT CTT CTG GCT CAG TCT GTT AAT CAG GGT TTT GAA GCC        1968
     Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln Gly Phe Glu Ala
                     645              650              655

     GTC TAT CAG CTA ACT AGA ATG TGC ACC ATA AGA ATG AGT TTT GTG AAA        2016
50   Val Tyr Gln Leu Thr Arg Met Cys Thr Ile Arg Met Ser Phe Val Lys
                     660              665              670

     GGG TGG GGA GCA GAA TAC CGA AGG CAG ACG GTA ACA AGT ACT CCT TGC        2064
     Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr Ser Thr Pro Cys
55                   675              680              685
```

101

102

```
      TGG ATT GAA CTT CAT CTG AAT GGA CCT CTA CAG TGG TTG GAC AAA GTA    2112
      Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp Leu Asp Lys Val
          690                     695                 700

5     TTA ACT CAG ATG GGA TCC CCT TCA GTG CGT TGC TCA AGC ATG TCA TAA    2160
      Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser Ser Met Ser
      705                     710                 715
```

10   (2) INFORMATION FOR SEQ ID NO:51:

            (i) SEQUENCE CHARACTERISTICS:
                 (A) LENGTH: 719 amino acids
                 (B) TYPE: amino acid
15   (C) STRANDEDNESS: single
                 (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: protein
            (v) FRAGMENT TYPE: internal
20
            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

```
      Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1                   5                   10                  15
25    Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                      20                  25                  30
      Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                  35                  40                  45
      Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
30        50                  55                  60
      Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
      65                  70                  75                  80
      Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                      85                  90                  95
35    Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                      100                 105                 110
      Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
              115                 120                 125
      Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
40        130                 135                 140
      Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
      145                 150                 155                 160
      Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                      165                 170                 175
45    Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                      180                 185                 190
      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
              195                 200                 205
      Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
50        210                 215                 220
      Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
      225                 230                 235                 240
      Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ser Ser Ile
                      245                 250                 255
55    Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu Gly Trp Lys Lys
                      260                 265                 270
```

102

BNSDOCID: <WO___9845704A2_I_>

```
      Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu Gln Asn Gly Gln
          275                 280                 285
      Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu Val Lys Lys Leu
          290                 295                 300
5     Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala Ile Thr Thr Gln
          305                 310                 315                 320
      Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr Cys Ser Glu Ile
                      325                 330                 335
      Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp Asp Thr Thr Gly
10                    340                 345                 350
      Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp Gly Arg Leu Gln
                  355                 360                 365
      Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr Cys Arg Leu Trp
                  370                 375                 380
15    Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys Ala Ile Glu Asn
          385                 390                 395                 400
      Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val Cys Val Asn Pro
                      405                 410                 415
      Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro Pro Val Leu Val
20                    420                 425                 430
      Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro Leu Asp Asp Tyr
                  435                 440                 445
      Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala Gly Ile Glu Pro
                  450                 455                 460
25    Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly Tyr Ile Ser Glu
          465                 470                 475                 480
      Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser Met Asp Thr Gly
                      485                 490                 495
      Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro Val Asn His Ser
30                    500                 505                 510
      Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala Phe Trp Cys Ser
                  515                 520                 525
      Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu Thr Phe His Ala
                  530                 535                 540
35    Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp Pro Ser Asn Ser
          545                 550                 555                 560
      Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn Arg Asn Ala Thr
                      565                 570.                575
      Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val Arg Leu Tyr Tyr
40                    580                 585                 590
      Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp Ser Ala Ile Phe
                  595                 600                 605
      Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp His Pro Ala Thr
                  610                 615                 620
45    Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile Phe Asn Asn Gln
          625                 630                 635                 640
      Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln Gly Phe Glu Ala
                      645                 650                 655
      Val Tyr Gln Leu Thr Arg Met Cys Thr Ile Arg Met Ser Phe Val Lys
50                    660                 665                 670
      Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr Ser Thr Pro Cys
                  675                 680                 685
      Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp Leu Asp Lys Val
                  690                 695                 700
55    Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser Ser Met Ser
          705                 710                 715
```

SUBSTITUTE SHEET (RULE 26)

(2) INFORMATION FOR SEQ ID NO:52:

    (i) SEQUENCE CHARACTERISTICS:
     (A) LENGTH: 2421 base pairs
     (B) TYPE: nucleic acid
     (C) STRANDEDNESS: single
     (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA
    (ix) FEATURE:

     (A) NAME/KEY: Coding Sequence
     (B) LOCATION: 1...2418
     (D) OTHER INFORMATION:

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
               100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
           115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
       130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
```

```
          145                      150                      155                      160

     GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC    528
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
  5                  165                      170                      175

     GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC    576
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                     180                      185                      190
 10

     CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                     195                      200                      205

 15  AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                     210                      215                      220

     GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
 20  Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                      230                      235                      240

     GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG AAT TCA ACC ATG GAC    768
     Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Asn Ser Thr Met Asp
 25                  245                      250                      255

     AAT ATG TCT ATT ACG AAT ACA CCA ACA AGT AAT GAT GCC TGT CTG AGC    816
     Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys Leu Ser
                     260                      265                      270
 30
     ATT GTG CAT AGT TTG ATG TGC CAT AGA CAA GGT GGA GAG AGT GAA ACA    864
     Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser Glu Thr
                     275                      280                      285

 35  TTT GCA AAA AGA GCA ATT GAA AGT TTG GTA AAG AAG CTG AAG GAG AAA    912
     Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys Glu Lys
                     290                      295                      300

     AAA GAT GAA TTG GAT TCT TTA ATA ACA GCT ATA ACT ACA AAT GGA GCT    960
 40  Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn Gly Ala
     305                      310                      315                      320

     CAT CCT AGT AAA TGT GTT ACC ATA CAG AGA ACA TTG GAT GGG AGG CTT   1008
     His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly Arg Leu
 45                  325                      330                      335

     CAG GTG GCT GGT CGG AAA GGA TTT CCT CAT GTG ATC TAT GCC CGT CTC   1056
     Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala Arg Leu
                     340                      345                      350
 50
     TGG AGG TGG CCT GAT CTT CAC AAA AAT GAA CTA AAA CAT GTT AAA TAT   1104
     Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val Lys Tyr
                     355                      360                      365

 55  TGT CAG TAT GCG TTT GAC TTA AAA TGT GAT AGT GTC TGT GTG AAT CCA   1152
     Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val Asn Pro
```

```
                370                    375                    380

       TAT CAC TAC GAA CGA GTT GTA TCA CCT GGA ATT GAT CTC TCA GGA TTA    1200
       Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser Gly Leu
  5    385                     390                    395                    400

       ACA CTG CAG AGT AAT GCT CCA TCA AGT ATG ATG GTG AAG GAT GAA TAT    1248
       Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp Glu Tyr
                           405                    410                    415
 10

       GTG CAT GAC TTT GAG GGA CAG CCA TCG TTG TCC ACT GAA GGA CAT TCA    1296
       Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly His Ser
                           420                    425                    430

 15    ATT CAA ACC ATC CAG CAT CCA CCA AGT AAT CGT GCA TCG ACA GAG ACA    1344
       Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr Glu Thr
                           435                    440                    445

       TAC AGC ACC CCA GCT CTG TTA GCC CCA TCT GAG TCT AAT GCT ACC AGC    1392
       Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala Thr Ser
 20                        450                    455                    460

       ACT GCC AAC TTT CCC AAC ATT CCT GTG GCT TCC ACA AGT CAG CCT GCC    1440
       Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln Pro Ala
 25    465                     470                    475                    480

       AGT ATA CTG GGG GGC AGC CAT AGT GAA GGA CTG TTG CAG ATA GCA TCA    1488
       Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile Ala Ser
                           485                    490                    495
 30

       GGG CCT CAG CCA GGA CAG CAG CAG AAT GGA TTT ACT GGT CAG CCA GCT    1536
       Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Gly Gln Pro Ala
                           500                    505                    510

 35    ACT TAC CAT CAT AAC AGC ACT ACC ACC TGG ACT GGA AGT AGG ACT GCA    1584
       Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg Thr Ala
                           515                    520                    525

       CCA TAC ACA CCT AAT TTG CCT CAC CAC CAA AAC GGC CAT CTT CAG CAC    1632
 40    Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu Gln His
       530                     535                    540

       CAC CCG CCT ATG CCG CCC CAT CCC GGA CAT TAC TGG CCT GTT CAC AAT    1680
       His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val His Asn
 45    545                     550                    555                    560

       GAG CTT GCA TTC CAG CCT CCC ATT TCC AAT CAT CCT GCT CCT GAG TAT    1728
       Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Pro Ala Pro Glu Tyr
                           565                    570                    575
 50

       TGG TGT TCC ATT GCT TAC TTT GAA ATG GAT GTT CAG GTA GGA GAG ACA    1776
       Trp Cys Ser Ile Ala Tyr Phe Glu Met Asp Val Gln Val Gly Glu Thr
                           580                    585                    590

 55    TTT AAG GTT CCT TCA AGC TGC CCT ATT GTT ACT GTT GAT GGA TAC GTG    1824
       Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly Tyr Val
```

```
                595                    600                    605

    GAC CCT TCT GGA GGA GAT CGC TTT TGT TTG GGT CAA CTC TCC AAT GTC    1872
 5  Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser Asn Val
        610                 615                 620

    CAC AGG ACA GAA GCC ATT GAG AGA GCA AGG TTG CAC ATA GGC AAA GGT    1920
    His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly Lys Gly
10  625                 630                 635                 640

    GTG CAG TTG GAA TGT AAA GGT GAA GGT GAT GTT TGG GTC AGG TGC CTT    1968
    Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg Cys Leu
                    645                 650                 655

15  AGT GAC CAC GCG GTC TTT GTA CAG AGT TAC TAC TTA GAC AGA GAA GCT    2016
    Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg Glu Ala
                660                 665                 670

    GGG CGT GCA CCT GGA GAT GCT GTT CAT AAG ATC TAC CCA AGT GCA TAT    2064
20  Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser Ala Tyr
                675                 680                 685

    ATA AAG GTC TTT GAT TTG CGT CAG TGT CAT CGA CAG ATG CAG CAG CAG    2112
    Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln Gln Gln
25      690                 695                 700

    GCG GCT ACT GCA CAA GCT GCA GCA GCT GCC CAG GCA GCA GCC GTG GCA    2160
    Ala Ala Thr Ala Gln Ala Ala Ala Ala Ala Gln Ala Ala Ala Val Ala
    705                 710                 715                 720
30
    GGA AAC ATC CCT GGC CCA GGA TCA GTA GGT GGA ATA GCT CCA GCT ATC    2208
    Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro Ala Ile
                    725                 730                 735

35  AGT CTG TCA GCT GCT GCT GGA ATT GGT GTT GAT GAC CTT CGT CGC TTA    2256
    Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg Arg Leu
                740                 745                 750

    TGC ATA CTC AGG ATG AGT TTT GTG AAA GGC TGG GGA CCG GAT TAC CCA    2304
40  Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp Tyr Pro
                755                 760                 765

    AGA CAG AGC ATC AAA GAA ACA CCT TGC TGG ATT GAA ATT CAC TTA CAC    2352
    Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His Leu His
45      770                 775                 780

    CGG GCC CTC CAG CTC CTA GAC GAA GTA CTT CAT ACC ATG CCG ATT GCA    2400
    Arg Ala Leu Gln Leu Leu Asp Glu Val Leu His Thr Met Pro Ile Ala
    785                 790                 795                 800
50
    GAC CCA CAA CCT TTA GAC TGA                                        2421
    Asp Pro Gln Pro Leu Asp
                805

55
                (2) INFORMATION FOR SEQ ID NO:53:
```

107

108

```
          (i) SEQUENCE CHARACTERISTICS:
             (A) LENGTH: 806 amino acids
             (B) TYPE: amino acid
  5          (C) STRANDEDNESS: single
             (D) TOPOLOGY: linear


         (ii) MOLECULE TYPE: protein
          (v) FRAGMENT TYPE: internal
 10

         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:


     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                   10                  15
 15  Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                     20                  25                  30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                     35                  40                  45
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 20          50                  55                  60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                     85                  90                  95
 25  Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100                 105                 110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                    115                 120                 125
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 30          130                 135                 140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                    165                 170                 175
 35  Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                    180                 185                 190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                    195                 200                 205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
 40          210                 215                 220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240
     Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Asn Ser Thr Met Asp
                    245                 250                 255
 45  Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys Leu Ser
                    260                 265                 270
     Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser Glu Thr
                    275                 280                 285
     Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys Glu Lys
 50          290                 295                 300
     Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn Gly Ala
     305                 310                 315                 320
     His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly Arg Leu
                    325                 330                 335
 55  Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala Arg Leu
                    340                 345                 350
```

```
      Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val Lys Tyr
          355                     360                 365
      Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val Asn Pro
          370                 375                 380
 5    Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser Gly Leu
          385             390                 395                 400
      Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp Glu Tyr
                      405                 410                 415
      Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly His Ser
10                    420                 425                 430
      Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr Glu Thr
              435                 440                 445
      Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala Thr Ser
          450                 455                 460
15    Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln Pro Ala
      465                 470                 475                 480
      Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile Ala Ser
                  485                 490                 495
      Gly Pro Gln Pro Gly Gln Gln Asn Gly Phe Thr Gly Gln Pro Ala
20                500                 505                 510
      Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg Thr Ala
          515                 520                 525
      Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu Gln His
          530                 535                 540
25    His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val His Asn
      545                 550                 555                 560
      Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Pro Ala Pro Glu Tyr
                  565                 570                 575
      Trp Cys Ser Ile Ala Tyr Phe Glu Met Asp Val Gln Val Gly Glu Thr
30                580                 585                 590
      Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly Tyr Val
          595                 600                 605
      Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser Asn Val
          610                 615                 620
35    His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly Lys Gly
      625                 630                 635                 640
      Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg Cys Leu
                  645                 650                 655
      Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg Glu Ala
40                660                 665                 670
      Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser Ala Tyr
          675                 680                 685
      Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln Gln Gln
          690                 695                 700
45    Ala Ala Thr Ala Gln Ala Ala Ala Ala Gln Ala Ala Ala Val Ala
      705                 710                 715                 720
      Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro Ala Ile
                  725                 730                 735
      Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg Arg Leu
50                740                 745                 750
      Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp Tyr Pro
          755                 760                 765
      Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His Leu His
          770                 775                 780
55    Arg Ala Leu Gln Leu Leu Asp Glu Val Leu His Thr Met Pro Ile Ala
      785                 790                 795                 800
```

SUBSTITUTE SHEET (RULE 26)

110

Asp Pro Gln Pro Leu Asp
                805

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 3120 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

    (A) NAME/KEY: Coding Sequence
    (B) LOCATION: 1...3117
    (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG     48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC     96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC    144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC    192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG    240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG    288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG    336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC    384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
            115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC    432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
        130                 135                 140
```

BNSDOCID: <WO___9845704A2_I_>

111

```
        AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC      480
        Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
        145             150             155             160

   5    GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
        Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                        165             170             175

        GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
   10   Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                    180             185             190

        CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
        Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
   15           195             200             205

        AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
        Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                210             215             220
   20
        GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
        Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
        225             230             235             240

   25   GGA CTC AGA TCT ACC ATG GCG GGC TGG ATC CAG GCC CAG CAG CTG CAG      768
        Gly Leu Arg Ser Thr Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln
                        245             250             255

        GGA GAC GCG CTG CGC CAG ATG CAG GTG CTG TAC GGC CAG CAC TTC CCC      816
   30   Gly Asp Ala Leu Arg Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro
                    260             265             270

        ATC GAG GTC CGG CAC TAC TTG GCC CAG TGG ATT GAG AGC CAG CCA TGG      864
        Ile Glu Val Arg His Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp
   35           275             280             285

        GAT GCC ATT GAC TTG GAC AAT CCC CAG GAC AGA GCC CAA GCC ACC CAG      912
        Asp Ala Ile Asp Leu Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln
                290             295             300
   40
        CTC CTG GAG GGC CTG GTG CAG GAG CTG CAG AAG AAG GCG GAG CAC CAG      960
        Leu Leu Glu Gly Leu Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln
        305             310             315             320

   45   GTG GGG GAA GAT GGG TTT TTA CTG AAG ATC AAG CTG GGG CAC TAC GCC     1008
        Val Gly Glu Asp Gly Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala
                        325             330             335

        ACG CAG CTC CAG AAA ACA TAT GAC CGC TGC CCC CTG GAG CTG GTC CGC     1056
   50   Thr Gln Leu Gln Lys Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg
                    340             345             350

        TGC ATC CGG CAC ATT CTG TAC AAT GAA CAG AGG CTG GTC CGA GAA GCC     1104
        Cys Ile Arg His Ile Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala
   55           355             360             365
```

111

112

```
    AAC AAT TGC AGC TCT CCG GCT GGG ATC CTG GTT GAC GCC ATG TCC CAG    1152
    Asn Asn Cys Ser Ser Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln
        370             375             380

 5  AAG CAC CTT CAG ATC AAC CAG ACA TTT GAG GAG CTG CGA CTG GTC ACG    1200
    Lys His Leu Gln Ile Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr
    385             390             395             400

    CAG GAC ACA GAG AAT GAG CTG AAG AAA CTG CAG CAG ACT CAG GAG TAC    1248
10  Gln Asp Thr Glu Asn Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr
                405             410             415

    TTC ATC ATC CAG TAC CAG GAG AGC CTG AGG ATC CAA GCT CAG TTT GCC    1296
    Phe Ile Ile Gln Tyr Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala
15              420             425             430

    CAG CTG GCC CAG CTG AGC CCC CAG GAG CGT CTG AGC CGG GAG ACG GCC    1344
    Gln Leu Ala Gln Leu Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala
            435             440             445
20
    CTC CAG CAG AAG CAG GTG TCT CTG GAG GCC TGG TTG CAG CGT GAG GCA    1392
    Leu Gln Gln Lys Gln Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala
        450             455             460

25  CAG ACA CTG CAG CAG TAC CGC GTG GAG CTG GCC GAG AAG CAC CAG AAG    1440
    Gln Thr Leu Gln Gln Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys
    465             470             475             480

    ACC CTG CAG CTG CTG CGG AAG CAG CAG ACC ATC ATC CTG GAT GAC GAG    1488
30  Thr Leu Gln Leu Leu Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu
                485             490             495

    CTG ATC CAG TGG AAG CGG CGG CAG CAG CTG GCC GGG AAC GGC GGG CCC    1536
    Leu Ile Gln Trp Lys Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro
35              500             505             510

    CCC GAG GGC AGC CTG GAC GTG CTA CAG TCC TGG TGT GAG AAG TTG GCC    1584
    Pro Glu Gly Ser Leu Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala
            515             520             525
40
    GAG ATC ATC TGG CAG AAC CGG CAG CAG ATC CGC AGG GCT GAG CAC CTC    1632
    Glu Ile Ile Trp Gln Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu
        530             535             540

45  TGC CAG CAG CTG CCC ATC CCC GGC CCA GTG GAG GAG ATG CTG GCC GAG    1680
    Cys Gln Gln Leu Pro Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu
    545             550             555             560

    GTC AAC GCC ACC ATC ACG GAC ATT ATC TCA GCC CTG GTG ACC AGC ACA    1728
50  Val Asn Ala Thr Ile Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr
                565             570             575

    TTC ATC ATT GAG AAG CAG CCT CCT CAG GTC CTG AAG ACC CAG ACC AAG    1776
    Phe Ile Ile Glu Lys Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys
55              580             585             590
```

112

```
    TTT GCA GCC ACC GTA CGC CTG CTG GTG GGC GGG AAG CTG AAC GTG CAC        1824
    Phe Ala Ala Thr Val Arg Leu Leu Val Gly Gly Lys Leu Asn Val His
            595                 600                 605

5   ATG AAT CCC CCC CAG GTG AAG GCC ACC ATC ATC AGT GAG CAG CAG GCC        1872
    Met Asn Pro Pro Gln Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala
            610                 615                 620

10  AAG TCT CTG CTT AAA AAT GAG AAC ACC CGC AAC GAG TGC AGT GGT GAG        1920
    Lys Ser Leu Leu Lys Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu
    625                 630                 635                 640

    ATC CTG AAC AAC TGC TGC GTG ATG GAG TAC CAC CAA GCC ACG GGC ACC        1968
    Ile Leu Asn Asn Cys Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr
15                  645                 650                 655

    CTC AGT GCC CAC TTC AGG AAC ATG TCA CTG AAG AGG ATC AAG CGT GCT        2016
    Leu Ser Ala His Phe Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala
                660                 665                 670
20
    GAC CGG CGG GGT GCA GAG TCC GTG ACA GAG GAG AAG TTC ACA GTC CTG        2064
    Asp Arg Arg Gly Ala Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu
                675                 680                 685

25  TTT GAG TCT CAG TTC AGT GTT GGC AGC AAT GAG CTT GTG TTC CAG GTG        2112
    Phe Glu Ser Gln Phe Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val
            690                 695                 700

    AAG ACT CTG TCC CTA CCT GTG GTT GTC ATC GTC CAC GGC AGC CAG GAC        2160
30  Lys Thr Leu Ser Leu Pro Val Val Val Ile Val His Gly Ser Gln Asp
    705                 710                 715                 720

    CAC AAT GCC ACG GCT ACT GTG CTG TGG GAC AAT GCC TTT GCT GAG CCG        2208
    His Asn Ala Thr Ala Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro
                725                 730                 735
35
    GGC AGG GTG CCA TTT GCC GTG CCT GAC AAA GTG CTG TGG CCG CAG CTG        2256
    Gly Arg Val Pro Phe Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu
                740                 745                 750
40
    TGT GAG GCG CTC AAC ATG AAA TTC AAG GCC GAA GTG CAG AGC AAC CGG        2304
    Cys Glu Ala Leu Asn Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg
                755                 760                 765

45  GGC CTG ACC AAG GAG AAC CTC GTG TTC CTG GCG CAG AAA CTG TTC AAC        2352
    Gly Leu Thr Lys Glu Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn
            770                 775                 780

    AAC AGC AGC AGC CAC CTG GAG GAC TAC AGT GGC CTG TCC GTG TCC TGG        2400
50  Asn Ser Ser Ser His Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp
    785                 790                 795                 800

    TCC CAG TTC AAC AGG GAG AAC TTG CCG GGC TGG AAC TAC ACC TTC TGG        2448
    Ser Gln Phe Asn Arg Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp
55                  805                 810                 815
```

113

114

```
     CAG TGG TTT GAC GGG GTG ATG GAG GTG TTG AAG AAG CAC CAC AAG CCC    2496
     Gln Trp Phe Asp Gly Val Met Glu Val Leu Lys Lys His His Lys Pro
                 820                 825                 830

 5   CAC TGG AAT GAT GGG GCC ATC CTA GGT TTT GTG AAT AAG CAA CAG GCC    2544
     His Trp Asn Asp Gly Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala
                 835                 840                 845

10   CAC GAC CTG CTC ATC AAC AAG CCC GAC GGG ACC TTC TTG TTG CGC TTT    2592
     His Asp Leu Leu Ile Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe
                 850                 855                 860

     AGT GAC TCA GAA ATC GGG GGC ATC ACC ATC GCC TGG AAG TTT GAC TCC    2640
     Ser Asp Ser Glu Ile Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser
15   865                 870                 875                 880

     CCG GAA CGC AAC CTG TGG AAC CTG AAA CCA TTC ACC ACG CGG GAT TTC    2688
     Pro Glu Arg Asn Leu Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe
                     885                 890                 895
20
     TCC ATC AGG TCC CTG GCT GAC CGG CTG GGG GAC CTG AGC TAT CTC ATC    2736
     Ser Ile Arg Ser Leu Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile
                     900                 905                 910

25   TAT GTG TTT CCT GAC CGC CCC AAG GAT GAG GTC TTC TCC AAG TAC TAC    2784
     Tyr Val Phe Pro Asp Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr
                 915                 920                 925

     ACT CCT GTG CTG GCT AAA GCT GTT GAT GGA TAT GTG AAA CCA CAG ATC    2832
30   Thr Pro Val Leu Ala Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile
                 930                 935                 940

     AAG CAA GTG GTC CCT GAG TTT GTG AAT GCA TCT GCA GAT GCT GGG GGC    2880
     Lys Gln Val Val Pro Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly
35   945                 950                 955                 960

     AGC AGC GCC ACG TAC ATG GAC CAG GCC CCC TCC CCA GCT GTG TGC CCC    2928
     Ser Ser Ala Thr Tyr Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro
                     965                 970                 975
40
     CAG GCT CCC TAT AAC ATG TAC CCA CAG AAC CCT GAC CAT GTA CTC GAT    2976
     Gln Ala Pro Tyr Asn Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp
                 980                 985                 990

45   CAG GAT GGA GAA TTC GAC CTG GAT GAG ACC ATG GAT GTG GCC AGG CAC    3024
     Gln Asp Gly Glu Phe Asp Leu Asp Glu Thr Met Asp Val Ala Arg His
                 995                 1000                1005

     GTG GAG GAA CTC TTA CGC CGA CCA ATG GAC AGT CTT GAC TCC CGC CTC    3072
50   Val Glu Glu Leu Leu Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu
                 1010                1015                1020

     TCG CCC CCT GCC GGT CTT TTC ACC TCT GCC AGA GGC TCC CTC TCA TGA    3120
     Ser Pro Pro Ala Gly Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser
55   1025                1030                1035                1
```

114

BNSDOCID: <WO___9845704A2_I_>

(2) INFORMATION FOR SEQ ID NO:55:

5
    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 1039 amino acids
       (B) TYPE: amino acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

10
    (ii) MOLECULE TYPE: protein
    (v) FRAGMENT TYPE: internal

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

```
15   Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                  10                  15
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                    20                  25                  30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
20                  35                  40                  45
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                    50                  55                  60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80
25   Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                         85                  90                  95
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                        100                 105                 110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
30                  115                 120                 125
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                    130                 135                 140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160
35   Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                        165                 170                 175
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                    180                 185                 190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
40                  195                 200                 205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                    210                 215                 220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240
45   Gly Leu Arg Ser Thr Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln
                    245                 250                 255
     Gly Asp Ala Leu Arg Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro
                    260                 265                 270
     Ile Glu Val Arg His Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp
50                  275                 280                 285
     Asp Ala Ile Asp Leu Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln
                    290                 295                 300
     Leu Leu Glu Gly Leu Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln
     305                 310                 315                 320
55   Val Gly Glu Asp Gly Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala
                    325                 330                 335
```

116

```
       Thr Gln Leu Gln Lys Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg
               340                     345                 350
       Cys Ile Arg His Ile Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala
               355                     360                 365
  5    Asn Asn Cys Ser Ser Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln
               370                 375                 380
       Lys His Leu Gln Ile Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr
       385                     390                 395                 400
       Gln Asp Thr Glu Asn Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr
 10                        405                 410                 415
       Phe Ile Ile Gln Tyr Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala
               420                     425                 430
       Gln Leu Ala Gln Leu Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala
               435                 440                     445
 15    Leu Gln Gln Lys Gln Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala
               450                     455                 460
       Gln Thr Leu Gln Gln Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys
       465                     470                 475                 480
       Thr Leu Gln Leu Leu Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu
 20                        485                 490                 495
       Leu Ile Gln Trp Lys Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro
               500                     505                 510
       Pro Glu Gly Ser Leu Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala
               515                 520                     525
 25    Glu Ile Ile Trp Gln Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu
               530                     535                 540
       Cys Gln Gln Leu Pro Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu
       545                 550                     555                 560
       Val Asn Ala Thr Ile Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr
 30                        565                 570                 575
       Phe Ile Ile Glu Lys Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys
               580                     585                 590
       Phe Ala Ala Thr Val Arg Leu Leu Val Gly Gly Lys Leu Asn Val His
               595                 600                     605
 35    Met Asn Pro Pro Gln Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala
           610                     615                 620
       Lys Ser Leu Leu Lys Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu
       625                 630                     635                 640
       Ile Leu Asn Asn Cys Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr
 40                        645                 650                 655
       Leu Ser Ala His Phe Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala
               660                     665                 670
       Asp Arg Arg Gly Ala Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu
               675                 680                     685
 45    Phe Glu Ser Gln Phe Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val
           690                     695                 700
       Lys Thr Leu Ser Leu Pro Val Val Val Ile Val His Gly Ser Gln Asp
       705                     710                 715                 720
       His Asn Ala Thr Ala Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro
 50                        725                     730                 735
       Gly Arg Val Pro Phe Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu
               740                     745                 750
       Cys Glu Ala Leu Asn Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg
               755                 760                     765
 55    Gly Leu Thr Lys Glu Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn
               770                     775                 780
```

BNSDOCID: <WO___9845704A2_I_>

```
   Asn Ser Ser Ser His Leu Glu Asp Tyr Ser ( y Leu Ser Val Ser Trp
   785             790             795                 800
   Ser Gln Phe Asn Arg Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp
               805             810             815
5  Gln Trp Phe Asp Gly Val Met Glu Val Leu Lys Lys His His Lys Pro
               820             825             830
   His Trp Asn Asp Gly Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala
           835             840             845
10 His Asp Leu Leu Ile Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe
       850             855             860
   Ser Asp Ser Glu Ile Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser
   865             870             875                 880
   Pro Glu Arg Asn Leu Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe
               885             890             895
15 Ser Ile Arg Ser Leu Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile
               900             905             910
   Tyr Val Phe Pro Asp Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr
           915             920             925
   Thr Pro Val Leu Ala Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile
20     930             935             940
   Lys Gln Val Val Pro Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly
   945             950             955                 960
   Ser Ser Ala Thr Tyr Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro
               965             970             975
25 Gln Ala Pro Tyr Asn Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp
           980             985             990
   Gln Asp Gly Glu Phe Asp Leu Asp Glu Thr Met Asp Val Ala Arg His
           995             1000            1005
   Val Glu Glu Leu Leu Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu
30     1010            1015            1020
   Ser Pro Pro Ala Gly Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser
   025             1030            1035                1
```

        (2) INFORMATION FOR SEQ ID NO:56:

35

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 1875 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
40   (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: cDNA
        (ix) FEATURE:

45   (A) NAME/KEY: Coding Sequence
            (B) LOCATION: 1...1872
            (D) OTHER INFORMATION:

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:
50

```
   ATG GCG GCG GCG GCG GCG GCT CCG GGG GGC GGG GGC GGG GAG CCC AGG    48
   Met Ala Ala Ala Ala Ala Ala Pro Gly Gly Gly Gly Gly Glu Pro Arg
   1               5               10              15
```

55
```
   GGA ACT GCT GGG GTC GTC CCG GTG GTC CCC GGG GAG GTG GAG GTG GTG    96
   Gly Thr Ala Gly Val Val Pro Val Val Pro Gly Glu Val Glu Val Val
```

117

118

```
                        20                         25                         30

        AAG GGG CAG CCA TTC GAT GTG GGC CCA CGC TAC ACG CAG CTG CAG TAC      144
        Lys Gly Gln Pro Phe Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr
5                   35                  40                  45

        ATC GGC GAG GGC GCG TAC GGC ATG GTC AGC TCA GCT TAT GAC CAC GTG      192
        Ile Gly Glu Gly Ala Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val
                    50                  55                  60
10

        CGC AAG ACC AGA GTG GCC ATC AAG AAG ATC AGC CCC TTT GAG CAT CAA      240
        Arg Lys Thr Arg Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln
        65                  70                  75                  80

15      ACC TAC TGT CAG CGC ACG CTG AGG GAG ATC CAG ATC TTG CTG CGA TTC      288
        Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe
                            85                  90                  95

        CGC CAT GAG AAT GTT ATA GGC ATC CGA GAC ATC CTC AGA GCG CCC ACC      336
        Arg His Glu Asn Val Ile Gly Ile Arg Asp Ile Leu Arg Ala Pro Thr
20                      100                 105                 110

        CTG GAA GCC ATG AGA GAT GTT TAC ATT GTT CAG GAC CTC ATG GAG ACA      384
        Leu Glu Ala Met Arg Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr
25                  115                 120                 125

        GAC CTG TAC AAG CTG CTT AAA AGC CAG CAG CTG AGC AAT GAC CAC ATC      432
        Asp Leu Tyr Lys Leu Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile
                    130                 135                 140
30

        TGC TAC TTC CTC TAC CAG ATC CTC CGG GGC CTC AAG TAT ATA CAC TCA      480
        Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser
        145                 150                 155                 160

35      GCC AAT GTG CTG CAC CGG GAC CTG AAG CCT TCC AAT CTG CTT ATC AAC      528
        Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu Leu Ile Asn
                            165                 170                 175

        ACC ACC TGC GAC CTT AAG ATC TGT GAT TTT GGC CTG GCC CGG ATT GCT      576
        Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala
40                      180                 185                 190

        GAC CCT GAG CAC GAC CAC ACT GGC TTT CTG ACG GAG TAT GTG GCC ACA      624
        Asp Pro Glu His Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr
45                  195                 200                 205

        CGC TGG TAC CGA GCC CCA GAG ATC ATG CTT AAT TCC AAG GGC TAC ACC      672
        Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr
                    210                 215                 220
50

        AAA TCC ATC GAC ATC TGG TCT GTG GGC TGC ATT CTG GCT GAG ATG CTC      720
        Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu
        225                 230                 235                 240

55      TCC AAC CGG CCC ATC TTC CCC GGC AAG CAC TAC CTG GAC CAG CTC AAC      768
        Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn
```

SUBSTITUTE SHEET (RULE 26)

119

245   250   255

```
      CAC ATT CTA GGT ATC TTG GGT TCC CCA TCC CAG GAG GAC CTT AAT TGC    816
      His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys
5             260                 265                 270

      ATC ATT AAC ATG AAG GCC CGA AAC TAC CTG CAG TCT CTG CCC TCG AAA    864
      Ile Ile Asn Met Lys Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys
              275                 280                 285
10

      ACC AAG GTG GCT TGG GCC AAG CTC TTT CCT AAA TCT GAC TCC AAA GCT    912
      Thr Lys Val Ala Trp Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala
          290                 295                 300

15    CTT GAC CTG CTG GAC CGG ATG TTA ACC TTC AAC CCA AAC AAG CGC ATC    960
      Leu Asp Leu Leu Asp Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile
      305                 310                 315                 320

      ACA GTA GAG GAA GCG CTG GCT CAC CCT TAC CTG GAA CAG TAC TAC GAT   1008
20    Thr Val Glu Glu Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp
                          325                 330                 335

      CCG ACA GAT GAG CCA GTG GCC GAG GAG CCA TTC ACC TTC GAC ATG GAG   1056
      Pro Thr Asp Glu Pro Val Ala Glu Glu Pro Phe Thr Phe Asp Met Glu
25                340                 345                 350

      CTG GAT GAC CTC CCC AAG GAG CGG CTG AAG GAG TTG ATC TTC CAG GAG   1104
      Leu Asp Asp Leu Pro Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu
                  355                 360                 365
30
      ACA GCC CGC TTC CAG CCA GGG GCG CCA GAG GGC CCC GGG CGC GCC ATG   1152
      Thr Ala Arg Phe Gln Pro Gly Ala Pro Glu Gly Pro Gly Arg Ala Met
              370                 375                 380

35    AGT AAA GGA GAA GAA CTT TTC ACT GGA GTT GTC CCA ATT CTT GTT GAA   1200
      Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
      385                 390                 395                 400

      TTA GAT GGC GAT GTT AAT GGG CAA AAA TTC TCT GTT AGT GGA GAG GGT   1248
40    Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser Gly Glu Gly
                      405                 410                 415

      GAA GGT GAT GCA ACA TAC GGA AAA CTT ACC CTT AAA TTT ATT TGC ACT   1296
      Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
45                420                 425                 430

      ACT GGG AAG CTA CCT GTT CCA TGG CCA ACG CTT GTC ACT ACT CTC ACT   1344
      Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
              435                 440                 445
50
      TAT GGT GTT CAA TGC TTT TCT AGA TAC CCA GAT CAT ATG AAA CAG CAT   1392
      Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
              450                 455                 460

55    GAC TTT TTC AAG AGT GCC ATG CCC GAA GGT TAT GTA CAG GAA AGA ACT   1440
      Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
```

119

SUBSTITUTE SHEET (RULE 26)

                                          120

         465   470   475   480

      ATA TTT TAC AAA GAT GAC GGG AAC TAC AAG ACA CGT GCT GAA GTC AAG   1488
      Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
 5   485   490   495

      TTT GAA GGT GAT ACC CTT GTT AAT AGA ATC GAG TTA AAA GGT ATT GAT   1536
      Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
                      500   505   510
 10

      TTT AAA GAA GAT GGA AAC ATT CTT GGA CAC AAA ATG GAA TAC AAT TAT   1584
      Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu Tyr Asn Tyr
                      515   520   525

 15   AAC TCA CAT AAT GTA TAC ATC ATG GCA GAC AAA CCA AAG AAT GGC ATC   1632
      Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys Asn Gly Ile
                      530   535   540

      AAA GTT AAC TTC AAA ATT AGA CAC AAC ATT AAA GAT GGA AGC GTT CAA   1680
 20   Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly Ser Val Gln
      545   550   555   560

      TTA GCA GAC CAT TAT CAA CAA AAT ACT CCA ATT GGC GAT GGC CCT GTC   1728
      Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                      565   570   575
 25

      CTT TTA CCA GAC AAC CAT TAC CTG TCC ACG CAA TCT GCC CTT TCC AAA   1776
      Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
                      580   585   590
 30

      GAT CCC AAC GAA AAG AGA GAT CAC ATG ATC CTT CTT GAG TTT GTA ACA   1824
      Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu Phe Val Thr
                      595   600   605

 35   GCT GCT GGG ATT ACA CAT GGC ATG GAT GAA CTA TAC AAA CCT CAG GAG T   1873
      Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys Pro Gln Glu
          610   615   620

      AA   1875
 40
                (2) INFORMATION FOR SEQ ID NO:57:

               (i) SEQUENCE CHARACTERISTICS:
                  (A) LENGTH: 624 amino acids
 45   (B) TYPE: amino acid
                  (C) STRANDEDNESS: single
                  (D) TOPOLOGY: linear

               (ii) MOLECULE TYPE: protein
 50   (v) FRAGMENT TYPE: internal

               (xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

      Met Ala Ala Ala Ala Ala Ala Pro Gly Gly Gly Gly Gly Glu Pro Arg
 55   1   5   10   15
      Gly Thr Ala Gly Val Val Pro Val Val Pro Gly Glu Val Glu Val Val

BNSDOCID: <WO___9845704A2_I_>

```
                  20                    25                    30
      Lys Gly Gln Pro Phe Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr
              35                    40                    45
      Ile Gly Glu Gly Ala Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val
  5           50                    55                    60
      Arg Lys Thr Arg Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln
      65                    70                    75                    80
      Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe
                  85                    90                    95
 10   Arg His Glu Asn Val Ile Gly Ile Arg Asp Ile Leu Arg Ala Pro Thr
                  100                   105                   110
      Leu Glu Ala Met Arg Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr
              115                   120                   125
      Asp Leu Tyr Lys Leu Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile
 15           130                   135                   140
      Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser
      145                   150                   155                   160
      Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu Leu Ile Asn
                  165                   170                   175
 20   Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala
                  180                   185                   190
      Asp Pro Glu His Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr
              195                   200                   205
      Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr
 25           210                   215                   220
      Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu
      225                   230                   235                   240
      Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn
                  245                   250                   255
 30   His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys
                  260                   265                   270
      Ile Ile Asn Met Lys Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys
              275                   280                   285
      Thr Lys Val Ala Trp Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala
 35           290                   295                   300
      Leu Asp Leu Leu Asp Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile
      305                   310                   315                   320
      Thr Val Glu Glu Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp
                  325                   330                   335
 40   Pro Thr Asp Glu Pro Val Ala Glu Glu Pro Phe Thr Phe Asp Met Glu
                  340                   345                   350
      Leu Asp Asp Leu Pro Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu
              355                   360                   365
      Thr Ala Arg Phe Gln Pro Gly Ala Pro Glu Gly Pro Gly Arg Ala Met
 45           370                   375                   380
      Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
      385                   390                   395                   400
      Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser Gly Glu Gly
                  405                   410                   415
 50   Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
                  420                   425                   430
      Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
              435                   440                   445
      Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
 55           450                   455                   460
      Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
```

SUBSTITUTE SHEET (RULE 26)

```
     465                      470                      475                      480
     Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
                     485                      490                      495
     Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
  5                  500                      505                      510
     Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu Tyr Asn Tyr
                     515                      520                      525
     Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys Asn Gly Ile
                     530                      535                      540
 10  Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly Ser Val Gln
     545                      550                      555                      560
     Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                     565                      570                      575
     Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
 15                  580                      585                      590
     Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu Phe Val Thr
                     595                      600                      605
     Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys Pro Gln Glu
                     610                      615                      620
 20
          (2)  INFORMATION FOR SEQ ID NO:58:

          (i)  SEQUENCE CHARACTERISTICS:
               (A)  LENGTH: 1815 base pairs
 25            (B)  TYPE: nucleic acid
               (C)  STRANDEDNESS: single
               (D)  TOPOLOGY: linear

          (ii)  MOLECULE TYPE: cDNA
 30       (ix)  FEATURE:

               (A)  NAME/KEY: Coding Sequence
               (B)  LOCATION: 1...1811
               (D)  OTHER INFORMATION:
 35
          (xi)  SEQUENCE DESCRIPTION: SEQ ID NO:58:

     ATG GCG GCG GCG GCG GCG GCG GGC CCG GAG ATG GTC CGC GGG CAG GTG      48
     Met Ala Ala Ala Ala Ala Ala Gly Pro Glu Met Val Arg Gly Gln Val
 40  1               5                   10                  15

     TTC GAC GTG GGG CCG CGC TAC ACT AAT CTC TCG TAC ATC GGA GAA GGC      96
     Phe Asp Val Gly Pro Arg Tyr Thr Asn Leu Ser Tyr Ile Gly Glu Gly
                     20                  25                  30
 45
     GCC TAC GGC ATG GTT TGT TCT GCT TAT GAT AAT CTC AAC AAA GTT CGA     144
     Ala Tyr Gly Met Val Cys Ser Ala Tyr Asp Asn Leu Asn Lys Val Arg
                     35                  40                  45

 50  GTT GCT ATC AAG AAA ATC AGT CCT TTT GAG CAC CAG ACC TAC TGT CAG     192
     Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln
                     50                  55                  60

     AGA ACC CTG AGA GAG ATA AAA ATC CTA CTG CGC TTC AGA CAT GAG AAC     240
 55  Arg Thr Leu Arg Glu Ile Lys Ile Leu Leu Arg Phe Arg His Glu Asn
     65                  70                  75                  80
```

122

BNSDOCID: <WO___9845704A2_I_>

```
       ATC ATC GGC ATC AAT GAC ATC ATC CGG GCA CCA ACC ATT GAG CAG ATG    288
       Ile Ile Gly Ile Asn Asp Ile Ile Arg Ala Pro Thr Ile Glu Gln Met
                         85              90              95
  5
       AAA GAT GTA TAT ATA GTA CAG GAC CTC ATG GAG ACA GAT CTT TAC AAG    336
       Lys Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys
                        100             105             110
 10    CTC TTG AAG ACA CAG CAC CTC AGC AAT GAT CAT ATC TGC TAT TTT CTT    384
       Leu Leu Lys Thr Gln His Leu Ser Asn Asp His Ile Cys Tyr Phe Leu
                    115             120             125

       TAT CAG ATC CTG AGA GGA TTA AAG TAT ATA CAT TCA GCT AAT GTT CTG    432
 15    Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu
                    130             135             140

       CAC CGT GAC CTC AAG CCT TCC AAC CTC CTG CTG AAC ACC ACT TGT GAT    480
       His Arg Asp Leu Lys Pro Ser Asn Leu Leu Leu Asn Thr Thr Cys Asp
 20    145             150             155             160

       CTC AAG ATC TGT GAC TTT GGC CTT GCC CGT GTT GCA GAT CCA GAC CAT    528
       Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Val Ala Asp Pro Asp His
                         165             170             175
 25
       GAT CAT ACA GGG TTC TTG ACA GAG TAT GTA GCC ACG CGT TGG TAC AGA    576
       Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg
                        180             185             190

 30    GCT CCA GAA ATT ATG TTG AAT TCC AAG GGT TAT ACC AAG TCC ATT GAT    624
       Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp
                    195             200             205

       ATT TGG TCT GTG GGC TGC ATC CTG GCA GAG ATG CTA TCC AAC AGG CCT    672
 35    Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro
                    210             215             220

       ATC TTC CCA GGA AAG CAT TAC CTT GAC CAG CTG AAT CAC ATC CTG GGT    720
       Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly
 40    225             230             235             240

       ATT CTT GGA TCT CCA TCA CAG GAA GAT CTG AAT TGT ATA ATA AAT TTA    768
       Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Leu
                         245             250             255
 45
       AAA GCT AGA AAC TAT TTG CTT TCT CTC CCG CAC AAA AAT AAG GTG CCG    816
       Lys Ala Arg Asn Tyr Leu Leu Ser Leu Pro His Lys Asn Lys Val Pro
                        260             265             270

 50    TGG AAC AGG TTG TTC CCA AAC GCT GAC TCC AAA GCT CTG GAT TTA CTG    864
       Trp Asn Arg Leu Phe Pro Asn Ala Asp Ser Lys Ala Leu Asp Leu Leu
                    275             280             285

       GAT AAA ATG TTG ACA TTT AAC CCT CAC AAG AGG ATT GAA GTT GAA CAG    912
 55    Asp Lys Met Leu Thr Phe Asn Pro His Lys Arg Ile Glu Val Glu Gln
                    290             295             300
```

SUBSTITUTE SHEET (RULE 26)

```
GCT CTG GCC CAC CCG TAC CTG GAG CAG TAT TAT GAC CCA AGT GAT GAG      960
Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Ser Asp Glu
305             310             315             320
```

```
CCC ATT GCT GAA GCA CCA TTC AAG TTT GAC ATG GAG CTG GAC GAC TTA     1008
Pro Ile Ala Glu Ala Pro Phe Lys Phe Asp Met Glu Leu Asp Asp Leu
                325             330             335
```

```
CCT AAG GAG AAG CTC AAA GAA CTC ATT TTT GAA GAG ACT GCT CGA TTC     1056
Pro Lys Glu Lys Leu Lys Glu Leu Ile Phe Glu Glu Thr Ala Arg Phe
            340             345             350
```

```
CAG CCA GGA TAC AGA TCT ATG GAT CCA CCG GTC GCC ACC ATG GTG AGC     1104
Gln Pro Gly Tyr Arg Ser Met Asp Pro Pro Val Ala Thr Met Val Ser
        355             360             365
```

```
AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG     1152
Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu
    370             375             380
```

```
GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG     1200
Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu
385             390             395             400
```

```
GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC     1248
Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr
            405             410             415
```

```
GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC     1296
Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr
            420             425             430
```

```
GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC     1344
Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp
        435             440             445
```

```
TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC     1392
Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile
    450             455             460
```

```
TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC     1440
Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe
465             470             475             480
```

```
GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC     1488
Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe
            485             490             495
```

```
AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC     1536
Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn
            500             505             510
```

```
AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG     1584
Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys
        515             520             525
```

SUBSTITUTE SHEET (RULE 26)

```
GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC    1632
Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu
    530                 535                 540

GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG    1680
Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu
545                 550                 555                 560

CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC    1728
Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp
                565                 570                 575

CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC    1776
Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala
                580                 585                 590

GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AA GTAA              1815
Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
                595                 600
```

       (2) INFORMATION FOR SEQ ID NO:59:

           (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 604 amino acids
               (B) TYPE: amino acid
               (C) STRANDEDNESS: single
               (D) TOPOLOGY: linear

           (ii) MOLECULE TYPE: protein
           (v) FRAGMENT TYPE: internal

           (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

```
Met Ala Ala Ala Ala Ala Ala Gly Pro Glu Met Val Arg Gly Gln Val
1                 5                 10                15
Phe Asp Val Gly Pro Arg Tyr Thr Asn Leu Ser Tyr Ile Gly Glu Gly
            20                25                30
Ala Tyr Gly Met Val Cys Ser Ala Tyr Asp Asn Leu Asn Lys Val Arg
        35                40                45
Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln
    50                55                60
Arg Thr Leu Arg Glu Ile Lys Ile Leu Leu Arg Phe Arg His Glu Asn
65                70                75                80
Ile Ile Gly Ile Asn Asp Ile Ile Arg Ala Pro Thr Ile Glu Gln Met
                85                90                95
Lys Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys
                100                105                110
Leu Leu Lys Thr Gln His Leu Ser Asn Asp His Ile Cys Tyr Phe Leu
        115                120                125
Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu
    130                135                140
His Arg Asp Leu Lys Pro Ser Asn Leu Leu Leu Asn Thr Thr Cys Asp
145                150                155                160
Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Val Ala Asp Pro Asp His
```

```
                    165                 170                 175
    Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg
                180                 185                 190
    Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp
 5          195                 200                 205
    Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro
            210                 215                 220
    Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly
    225                 230                 235                 240
10  Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Leu
                    245                 250                 255
    Lys Ala Arg Asn Tyr Leu Leu Ser Leu Pro His Lys Asn Lys Val Pro
                260                 265                 270
    Trp Asn Arg Leu Phe Pro Asn Ala Asp Ser Lys Ala Leu Asp Leu Leu
15              275                 280                 285
    Asp Lys Met Leu Thr Phe Asn Pro His Lys Arg Ile Glu Val Glu Gln
            290                 295                 300
    Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Ser Asp Glu
    305                 310                 315                 320
20  Pro Ile Ala Glu Ala Pro Phe Lys Phe Asp Met Glu Leu Asp Asp Leu
                    325                 330                 335
    Pro Lys Glu Lys Leu Lys Glu Leu Ile Phe Glu Glu Thr Ala Arg Phe
                340                 345                 350
    Gln Pro Gly Tyr Arg Ser Met Asp Pro Pro Val Ala Thr Met Val Ser
25              355                 360                 365
    Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu
            370                 375                 380
    Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu
    385                 390                 395                 400
30  Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr
                    405                 410                 415
    Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr
                420                 425                 430
    Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp
35              435                 440                 445
    Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile
            450                 455                 460
    Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe
    465                 470                 475                 480
40  Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe
                    485                 490                 495
    Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn
                500                 505                 510
    Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys
45              515                 520                 525
    Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu
            530                 535                 540
    Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu
    545                 550                 555                 560
50  Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp
                    565                 570                 575
    Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala
                580                 585                 590
    Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
55              595                 600
```

(2) INFORMATION FOR SEQ ID NO:60:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 2511 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA
    (ix) FEATURE:

       (A) NAME/KEY: Coding Sequence
       (B) LOCATION: 1...2508
       (D) OTHER INFORMATION:

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

```
ATG GAG CTG GAA AAC ATC GTG GCC AAC ACG GTC TTG CTG AAA GCC AGG     48
Met Glu Leu Glu Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg
1               5                   10                  15

GAA GGG GGC GGA GGA AAG CGC AAA GGG AAA AGC AAG AAG TGG AAA GAA     96
Glu Gly Gly Gly Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu
                20                  25                  30

ATC CTG AAG TTC CCT CAC ATT AGC CAG TGT GAA GAC CTC CGA AGG ACC    144
Ile Leu Lys Phe Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr
            35                  40                  45

ATA GAC AGA GAT TAC TGC AGT TTA TGT GAC AAG CAG CCA ATC GGG AGG    192
Ile Asp Arg Asp Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg
        50                  55                  60

CTG CTT TTC CGG CAG TTT TGT GAA ACC AGG CCT GGG CTG GAG TGT TAC    240
Leu Leu Phe Arg Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr
65                  70                  75                  80

ATT CAG TTC CTG GAC TCC GTG GCA GAA TAT GAA GTT ACT CCA GAT GAA    288
Ile Gln Phe Leu Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu
                85                  90                  95

AAA CTG GGA GAG AAA GGG AAG GAA ATT ATG ACC AAG TAC CTC ACC CCA    336
Lys Leu Gly Glu Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro
                100                 105                 110

AAG TCC CCT GTT TTC ATA GCC CAA GTT GGC CAA GAC CTG GTC TCC CAG    384
Lys Ser Pro Val Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln
            115                 120                 125

ACG GAG GAG AAG CTC CTA CAG AAG CCG TGC AAA GAA CTC TTT TCT GCC    432
Thr Glu Glu Lys Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala
        130                 135                 140

TGT GCA CAG TCT GTC CAC GAG TAC CTG AGG GGA GAA CCA TTC CAC GAA    480
Cys Ala Gln Ser Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu
145                 150                 155                 160
```

127

```
     TAT CTG GAC AGC ATG TTT TTT GAC CGC TTT CTC CAG TGG AAG TGG TTG    528
     Tyr Leu Asp Ser Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu
                 165             170             175
 5
     GAA AGG CAA CCG GTG ACC AAA AAC ACT TTC AGG CAG TAT CGA GTG CTA    576
     Glu Arg Gln Pro Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu
                 180             185             190

10   GGA AAA GGG GGC TTC GGG GAG GTC TGT GCC TGC CAG GTT CGG GCC ACG    624
     Gly Lys Gly Gly Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr
                 195             200             205

     GGT AAA ATG TAT GCC TGC AAG CGC TTG GAG AAG AAG AGG ATC AAA AAG    672
15   Gly Lys Met Tyr Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys
         210             215             220

     AGG AAA GGG GAG TCC ATG GCC CTC AAT GAG AAG CAG ATC CTC GAG AAG    720
     Arg Lys Gly Glu Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys
20   225             230             235             240

     GTC AAC AGT CAG TTT GTG GTC AAC CTG GCC TAT GCC TAC GAG ACC AAG    768
     Val Asn Ser Gln Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys
                 245             250             255
25
     GAT GCA CTG TGC TTG GTC CTG ACC ATC ATG AAT GGG GGT GAC CTG AAG    816
     Asp Ala Leu Cys Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys
                 260             265             270

30   TTC CAC ATC TAC AAC ATG GGC AAC CCT GGC TTC GAG GAG GAG CGG GCC    864
     Phe His Ile Tyr Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala
                 275             280             285

     TTG TTT TAT GCG GCA GAG ATC CTC TGC GGC TTA GAA GAC CTC CAC CGT    912
35   Leu Phe Tyr Ala Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg
         290             295             300

     GAG AAC ACC GTC TAC CGA GAT CTG AAA CCT GAA AAC ATC CTG TTA GAT    960
     Glu Asn Thr Val Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp
40   305             310             315             320

     GAT TAT GGC CAC ATT AGG ATC TCA GAC CTG GGC TTG GCT GTG AAG ATC   1008
     Asp Tyr Gly His Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile
                 325             330             335
45
     CCC GAG GGA GAC CTG ATC CGC GGC CGG GTG GGC ACT GTT GGC TAC ATG   1056
     Pro Glu Gly Asp Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met
                 340             345             350

50   GCC CCC GAA GTC CTG AAC AAC CAG AGG TAC GGC CTG AGC CCC GAC TAC   1104
     Ala Pro Glu Val Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr
                 355             360             365

     TGG GGC CTT GGC TGC CTC ATC TAT GAG ATG ATC GAG GGC CAG TCG CCG   1152
55   Trp Gly Leu Gly Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro
         370             375             380
```

```
   TTC CGC GGC CGT AAG GAG AAG GTG AAG CGG GAG GAG GTG GAC CGC CGG    1200
   Phe Arg Gly Arg Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg
   385             390             395             400
5
   GTC CTG GAG ACG GAG GAG GTG TAC TCC CAC AAG TTC TCC GAG GAG GCC    1248
   Val Leu Glu Thr Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala
                   405             410             415
10 AAG TCC ATC TGC AAG ATG CTG CTC ACG AAA GAT GCG AAG CAG AGG CTG    1296
   Lys Ser Ile Cys Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu
               420             425             430

   GGC TGC CAG GAG GAG GGG GCT GCA GAG GTC AAG AGA CAC CCC TTC TTC    1344
15 Gly Cys Gln Glu Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe
               435             440             445

   AGG AAC ATG AAC TTC AAG CGC TTA GAA GCC GGG ATG TTG GAC CCT CCC    1392
   Arg Asn Met Asn Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro
20 450             455             460

   TTC GTT CCA GAC CCC CGC GCT GTG TAC TGT AAG GAC GTG CTG GAC ATC    1440
   Phe Val Pro Asp Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile
   465             470             475             480
25
   GAG CAG TTC TCC ACT GTG AAG GGC GTC AAT CTG GAC CAC ACA GAC GAC    1488
   Glu Gln Phe Ser Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp
                   485             490             495

30 GAC TTC TAC TCC AAG TTC TCC ACG GGC TCT GTG TCC ATC CCA TGG CAA    1536
   Asp Phe Tyr Ser Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln
                   500             505             510

   AAC GAG ATG ATA GAA ACA GAA TGC TTT AAG GAG CTG AAC GTG TTT GGA    1584
35 Asn Glu Met Ile Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly
               515             520             525

   CCT AAT GGT ACC CTC CCG CCA GAT CTG AAC AGA AAC CAC CCT CCG GAA    1632
   Pro Asn Gly Thr Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu
40 530             535             540

   CCG CCC AAG AAA GGG CTG CTC CAG AGA CTC TTC AAG CGG CAG CAT CAG    1680
   Pro Pro Lys Lys Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln
   545             550             555             560
45
   AAC AAT TCC AAG AGT TCG CCC AGC TCC AAG ACC AGT TTT AAC CAC CAC    1728
   Asn Asn Ser Lys Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His
                   565             570             575

50 ATA AAC TCA AAC CAT GTC AGC TCG AAC TCC ACC GGA AGC AGC AGG GAT    1776
   Ile Asn Ser Asn His Val Ser Ser Asn Ser Thr Gly Ser Ser Arg Asp
                   580             585             590

   CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG    1824
55 Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
                   595             600             605
```

```
      GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG    1872
      Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
          610             615             620
  5
      TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG    1920
      Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
      625             630             635             640

 10   ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC    1968
      Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
                  645             650             655

      ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC    2016
 15   Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
                  660             665             670

      CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA    2064
      Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
 20               675             680             685

      GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC    2112
      Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
                  690             695             700
 25
      AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC    2160
      Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
      705             710             715             720

 30   ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG    2208
      Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
                  725             730             735

      CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC    2256
 35   His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
                  740             745             750

      GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC    2304
      Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
 40           755             760             765

      ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC    2352
      Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
          770             775             780
 45
      CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC    2400
      Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
      785             790             795             800

 50   ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG    2448
      Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
                  805             810             815

      GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC    2496
 55   Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
                  820             825             830
```

SUBSTITUTE SHEET (RULE 26)

```
GAG CTG TAC AAG TAA                                              2511
Glu Leu Tyr Lys
        835
```

5

        (2) INFORMATION FOR SEQ ID NO:61:

        (i) SEQUENCE CHARACTERISTICS:
10   (A) LENGTH: 836 amino acids
            (B) TYPE: amino acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

15   (ii) MOLECULE TYPE: protein
        (v) FRAGMENT TYPE: internal

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

```
20  Met Glu Leu Glu Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg
     1               5                  10                  15
    Glu Gly Gly Gly Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu
                    20                  25                  30
    Ile Leu Lys Phe Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr
25                  35                  40                  45
    Ile Asp Arg Asp Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg
                50                  55                  60
    Leu Leu Phe Arg Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr
    65                  70                  75                  80
30  Ile Gln Phe Leu Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu
                    85                  90                  95
    Lys Leu Gly Glu Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro
                    100                 105                 110
    Lys Ser Pro Val Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln
35                  115                 120                 125
    Thr Glu Glu Lys Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala
                    130                 135                 140
    Cys Ala Gln Ser Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu
    145                 150                 155                 160
40  Tyr Leu Asp Ser Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu
                        165                 170                 175
    Glu Arg Gln Pro Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu
                    180                 185                 190
    Gly Lys Gly Gly Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr
45                  195                 200                 205
    Gly Lys Met Tyr Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys
                    210                 215                 220
    Arg Lys Gly Glu Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys
    225                 230                 235                 240
50  Val Asn Ser Gln Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys
                        245                 250                 255
    Asp Ala Leu Cys Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys
                    260                 265                 270
    Phe His Ile Tyr Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala
55                  275                 280                 285
    Leu Phe Tyr Ala Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg
```

BNSDOCID: <WO___9845704A2_I_>

```
             290                    295                    300
     Glu Asn Thr Val Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp
     305                    310                    315                    320
     Asp Tyr Gly His Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile
  5                     325                    330                    335
     Pro Glu Gly Asp Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met
                     340                    345                    350
     Ala Pro Glu Val Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr
                     355                    360                    365
 10  Trp Gly Leu Gly Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro
                     370                    375                    380
     Phe Arg Gly Arg Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg
     385                    390                    395                    400
     Val Leu Glu Thr Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala
 15                     405                    410                    415
     Lys Ser Ile Cys Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu
                     420                    425                    430
     Gly Cys Gln Glu Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe
                     435                    440                    445
 20  Arg Asn Met Asn Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro
                     450                    455                    460
     Phe Val Pro Asp Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile
     465                    470                    475                    480
     Glu Gln Phe Ser Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp
 25                     485                    490                    495
     Asp Phe Tyr Ser Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln
                     500                    505                    510
     Asn Glu Met Ile Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly
                     515                    520                    525
 30  Pro Asn Gly Thr Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu
                     530                    535                    540
     Pro Pro Lys Lys Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln
     545                    550                    555                    560
     Asn Asn Ser Lys Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His
 35                     565                    570                    575
     Ile Asn Ser Asn His Val Ser Ser Asn Ser Thr Gly Ser Ser Arg Asp
                     580                    585                    590
     Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
                     595                    600                    605
 40  Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
                     610                    615                    620
     Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
     625                    630                    635                    640
     Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
 45                     645                    650                    655
     Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
                     660                    665                    670
     Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
                     675                    680                    685
 50  Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
                     690                    695                    700
     Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
     705                    710                    715                    720
     Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
 55                     725                    730                    735
     His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
```

```
                740                    745                    750
     Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
                755                    760                    765
     Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
  5          770                    775                    780
     Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
     785                    790                    795                    800
     Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
                805                    810                    815
 10  Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
                820                    825                    830
     Glu Leu Tyr Lys
                835
```

15   (2) INFORMATION FOR SEQ ID NO:62:

          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 1893 base pairs
               (B) TYPE: nucleic acid
20   (C) STRANDEDNESS: single
               (D) TOPOLOGY: linear

          (ii) MOLECULE TYPE: cDNA
          (ix) FEATURE:
25
               (A) NAME/KEY: Coding Sequence
               (B) LOCATION: 1...1890
               (D) OTHER INFORMATION:

30   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

```
     ATG AGC AGA AGC AAG CGT GAC AAC AAT TTT TAT AGT GTA GAG ATT GGA    48
     Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
       1               5                   10                  15
35
     GAT TCT ACA TTC ACA GTC CTG AAA CGA TAT CAG AAT TTA AAA CCT ATA    96
     Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
               20                  25                  30

40   GGC TCA GGA GCT CAA GGA ATA GTA TGC GCA GCT TAT GAT GCC ATT CTT   144
     Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
               35                  40                  45

     GAA AGA AAT GTT GCA ATC AAG AAG CTA AGC CGA CCA TTT CAG AAT CAG   192
45   Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
               50                  55                  60

     ACT CAT GCC AAG CGG GCC TAC AGA GAG CTA GTT CTT ATG AAA TGT GTT   240
     Thr His Ala Lys Arg Ala Tyr Arg Glu Leu Val Leu Met Lys Cys Val
50   65                  70                  75                  80

     AAT CAC AAA AAT ATA ATT GGC CTT TTG AAT GTT TTC ACA CCA CAG AAA   288
     Asn His Lys Asn Ile Ile Gly Leu Leu Asn Val Phe Thr Pro Gln Lys
                    85                  90                  95
55
     TCC CTA GAA GAA TTT CAA GAT GTT TAC ATA GTC ATG GAG CTC ATG GAT   336
```

133

```
        Ser Leu Glu Glu Phe Gln Asp Val Tyr Ile Val Met Glu Leu Met Asp
                    100                 105                 110

    5   GCA AAT CTT TGC CAA GTG ATT CAG ATG GAG CTA GAT CAT GAA AGA ATG      384
        Ala Asn Leu Cys Gln Val Ile Gln Met Glu Leu Asp His Glu Arg Met
                    115                 120                 125

   10   TCC TAC CTT CTC TAT CAG ATG CTG TGT GGA ATC AAG CAC CTT CAT TCT      432
        Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly Ile Lys His Leu His Ser
                    130                 135                 140

        GCT GGA ATT ATT CAT CGG GAC TTA AAG CCC AGT AAT ATA GTA GTA AAA      480
        Ala Gly Ile Ile His Arg Asp Leu Lys Pro Ser Asn Ile Val Val Lys
        145                 150                 155                 160
   15
        TCT GAT TGC ACT TTG AAG ATT CTT GAC TTC GGT CTG GCC AGG ACT GCA      528
        Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg Thr Ala
                        165                 170                 175

   20   GGA ACG AGT TTT ATG ATG ACG CCT TAT GTA GTG ACT CGC TAC TAC AGA      576
        Gly Thr Ser Phe Met Met Thr Pro Tyr Val Val Thr Arg Tyr Tyr Arg
                        180                 185                 190

        GCA CCC GAG GTC ATC CTT GGC ATG GGC TAC AAG GAA AAC GTG GAT TTA      624
   25   Ala Pro Glu Val Ile Leu Gly Met Gly Tyr Lys Glu Asn Val Asp Leu
                    195                 200                 205

        TGG TCT GTG GGG TGC ATT ATG GGA GAA ATG GTT TGC CAC AAA ATC CTC      672
        Trp Ser Val Gly Cys Ile Met Gly Glu Met Val Cys His Lys Ile Leu
   30       210                 215                 220

        TTT CCA GGA AGG GAC TAT ATT GAT CAG TGG AAT AAA GTT ATT GAA CAG      720
        Phe Pro Gly Arg Asp Tyr Ile Asp Gln Trp Asn Lys Val Ile Glu Gln
        225                 230                 235                 240
   35
        CTT GGA ACA CCA TGT CCT GAA TTC ATG AAG AAA CTG CAA CCA ACA GTA      768
        Leu Gly Thr Pro Cys Pro Glu Phe Met Lys Lys Leu Gln Pro Thr Val
                        245                 250                 255

   40   AGG ACT TAC GTT GAA AAC AGA CCT AAA TAT GCT GGA TAT AGC TTT GAG      816
        Arg Thr Tyr Val Glu Asn Arg Pro Lys Tyr Ala Gly Tyr Ser Phe Glu
                    260                 265                 270

        AAA CTC TTC CCT GAT GTC CTT TTC CCA GCT GAC TCA GAA CAC AAC AAA      864
   45   Lys Leu Phe Pro Asp Val Leu Phe Pro Ala Asp Ser Glu His Asn Lys
                    275                 280                 285

        CTT AAA GCC AGT CAG GCA AGG GAT TTG TTA TCC AAA ATG CTG GTA ATA      912
        Leu Lys Ala Ser Gln Ala Arg Asp Leu Leu Ser Lys Met Leu Val Ile
   50       290                 295                 300

        GAT GCA TCT AAA AGG ATC TCT GTA GAT GAA GCT CTC CAA CAC CCG TAC      960
        Asp Ala Ser Lys Arg Ile Ser Val Asp Glu Ala Leu Gln His Pro Tyr
        305                 310                 315                 320
   55
        ATC AAT GTC TGG TAT GAT CCT TCT GAA GCA GAA GCT CCA CCA CCA AAG     1008
```

BNSDOCID: <WO___9845704A2_I_>

135

```
        Ile Asn Val Trp Tyr Asp Pro Ser Glu Ala Glu Ala Pro Pro Pro Lys
                        325             330             335

  5     ATC CCT GAC AAG CAG TTA GAT GAA AGG GAA CAC ACA ATA GAA GAG TGG     1056
        Ile Pro Asp Lys Gln Leu Asp Glu Arg Glu His Thr Ile Glu Glu Trp
                    340             345             350

        AAA GAA TTG ATA TAT AAG GAA GTT ATG GAC TTG GAG GAG AGA ACC AAG     1104
 10     Lys Glu Leu Ile Tyr Lys Glu Val Met Asp Leu Glu Glu Arg Thr Lys
                    355             360             365

        AAT GGA GTT ATA CGG GGG CAG CCC TCT CCT TTA GCA CAG GTG CAG CAG     1152
        Asn Gly Val Ile Arg Gly Gln Pro Ser Pro Leu Ala Gln Val Gln Gln
                    370             375             380
 15
        TGG GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC     1200
        Trp Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe
        385                 390             395                 400

 20     ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC     1248
        Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly
                        405             410             415

        CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC     1296
 25     His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly
                    420             425             430

        AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC     1344
        Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro
 30                 435             440             445

        TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC     1392
        Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser
                    450             455             460
 35
        CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG     1440
        Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met
        465                 470             475                 480

 40     CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC     1488
        Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly
                        485             490             495

        AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG     1536
 45     Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val
                    500             505             510

        AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC     1584
        Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile
 50                 515             520             525

        CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC     1632
        Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile
                    530             535             540
 55
        ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC     1680
```

135

SUBSTITUTE SHEET (RULE 26)

136

```
      Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
      545             550             555             560

 5    CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG   1728
      His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
                      565             570             575

      AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC   1776
      Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
10                    580             585             590

      CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT   1824
      Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
                  595             600             605
15
      CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC   1872
      His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
                  610             615             620

20    ATG GAC GAG CTG TAC AAG TAA                                       1893
      Met Asp Glu Leu Tyr Lys
      625             630


25            (2) INFORMATION FOR SEQ ID NO:63:

          (i) SEQUENCE CHARACTERISTICS:
              (A) LENGTH: 630 amino acids
              (B) TYPE: amino acid
30            (C) STRANDEDNESS: single
              (D) TOPOLOGY: linear

          (ii) MOLECULE TYPE: protein
          (v) FRAGMENT TYPE: internal
35
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

      Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
      1               5               10              15
40    Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
                      20              25              30
      Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
                  35              40              45
      Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
45        50              55              60
      Thr His Ala Lys Arg Ala Tyr Arg Glu Leu Val Leu Met Lys Cys Val
      65              70              75              80
      Asn His Lys Asn Ile Ile Gly Leu Leu Asn Val Phe Thr Pro Gln Lys
                      85              90              95
50    Ser Leu Glu Glu Phe Gln Asp Val Tyr Ile Val Met Glu Leu Met Asp
                  100             105             110
      Ala Asn Leu Cys Gln Val Ile Gln Met Glu Leu Asp His Glu Arg Met
                  115             120             125
      Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly Ile Lys His Leu His Ser
55        130             135             140
      Ala Gly Ile Ile His Arg Asp Leu Lys Pro Ser Asn Ile Val Val Lys
```

136

```
        145                      150                      155                      160
        Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg Thr Ala
                        165                  170                      175
        Gly Thr Ser Phe Met Met Thr Pro Tyr Val Val Thr Arg Tyr Tyr Arg
5                           180                  185                  190
        Ala Pro Glu Val Ile Leu Gly Met Gly Tyr Lys Glu Asn Val Asp Leu
                    195                  200                  205
        Trp Ser Val Gly Cys Ile Met Gly Glu Met Val Cys His Lys Ile Leu
                210                  215                  220
10      Phe Pro Gly Arg Asp Tyr Ile Asp Gln Trp Asn Lys Val Ile Glu Gln
        225                  230                  235                  240
        Leu Gly Thr Pro Cys Pro Glu Phe Met Lys Lys Leu Gln Pro Thr Val
                        245                  250                      255
        Arg Thr Tyr Val Glu Asn Arg Pro Lys Tyr Ala Gly Tyr Ser Phe Glu
15                      260                  265                  270
        Lys Leu Phe Pro Asp Val Leu Phe Pro Ala Asp Ser Glu His Asn Lys
                275                  280                  285
        Leu Lys Ala Ser Gln Ala Arg Asp Leu Leu Ser Lys Met Leu Val Ile
                290                  295                  300
20      Asp Ala Ser Lys Arg Ile Ser Val Asp Glu Ala Leu Gln His Pro Tyr
        305                  310                  315                  320
        Ile Asn Val Trp Tyr Asp Pro Ser Glu Ala Glu Ala Pro Pro Pro Lys
                        325                  330                      335
        Ile Pro Asp Lys Gln Leu Asp Glu Arg Glu His Thr Ile Glu Glu Trp
25                      340                  345                  350
        Lys Glu Leu Ile Tyr Lys Glu Val Met Asp Leu Glu Glu Arg Thr Lys
                355                  360                  365
        Asn Gly Val Ile Arg Gly Gln Pro Ser Pro Leu Ala Gln Val Gln Gln
                370                  375                  380
30      Trp Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe
        385                  390                  395                  400
        Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly
                        405                  410                      415
        His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly
35                      420                  425                  430
        Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro
                435                  440                  445
        Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser
                450                  455                  460
40      Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met
        465                  470                  475                  480
        Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly
                        485                  490                      495
        Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val
45                      500                  505                  510
        Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile
                515                  520                  525
        Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile
                530                  535                  540
50      Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
        545                  550                  555                  560
        His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
                        565                  570                      575
        Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
55                      580                  585                  590
        Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
```

SUBSTITUTE SHEET (RULE 26)

```
                 595              600                 605
    His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
        610                 615                 620
    Met Asp Glu Leu Tyr Lys
5   625                 630


            (2) INFORMATION FOR SEQ ID NO:64:

            (i) SEQUENCE CHARACTERISTICS:
10              (A) LENGTH: 1821 base pairs
                (B) TYPE: nucleic acid
                (C) STRANDEDNESS: single
                (D) TOPOLOGY: linear

15          (ii) MOLECULE TYPE: cDNA
            (ix) FEATURE:

                (A) NAME/KEY: Coding Sequence
                (B) LOCATION: 1...1818
20              (D) OTHER INFORMATION:

            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:


    ATG TCT CAG GAG AGG CCC ACG TTC TAC CGG CAG GAG CTG AAC AAG ACA        48
25  Met Ser Gln Glu Arg Pro Thr Phe Tyr Arg Gln Glu Leu Asn Lys Thr
     1               5                  10                  15

    ATC TGG GAG GTG CCC GAG CGT TAC CAG AAC CTG TCT CCA GTG GGC TCT        96
    Ile Trp Glu Val Pro Glu Arg Tyr Gln Asn Leu Ser Pro Val Gly Ser
30              20                  25                  30

    GGC GCC TAT GGC TCT GTG TGT GCT GCT TTT GAC ACA AAA ACG GGG TTA       144
    Gly Ala Tyr Gly Ser Val Cys Ala Ala Phe Asp Thr Lys Thr Gly Leu
            35                  40                  45
35

    CGT GTG GCA GTG AAG AAG CTC TCC AGA CCA TTT CAG TCC ATC ATT CAT       192
    Arg Val Ala Val Lys Lys Leu Ser Arg Pro Phe Gln Ser Ile Ile His
        50                  55                  60

40  GCG AAA AGA ACC TAC AGA GAA CTG CGG TTA CTT AAA CAT ATG AAA CAT       240
    Ala Lys Arg Thr Tyr Arg Glu Leu Arg Leu Leu Lys His Met Lys His
    65                  70                  75                  80

    GAA AAT GTG ATT GGT CTG TTG GAC GTT TTT ACA CCT GCA AGG TCT CTG       288
45  Glu Asn Val Ile Gly Leu Leu Asp Val Phe Thr Pro Ala Arg Ser Leu
                        85                  90                  95

    GAG GAA TTC AAT GAT GTG TAT CTG GTG ACC CAT CTC ATG GGG GCA GAT       336
    Glu Glu Phe Asn Asp Val Tyr Leu Val Thr His Leu Met Gly Ala Asp
50                      100                 105                 110

    CTG AAC AAC ATT GTG AAA TGT CAG AAG CTT ACA GAT GAC CAT GTT CAG       384
    Leu Asn Asn Ile Val Lys Cys Gln Lys Leu Thr Asp Asp His Val Gln
                    115                 120                 125
55
    TTC CTT ATC TAC CAA ATT CTC CGA GGT CTA AAG TAT ATA CAT TCA GCT       432
```

```
      Phe Leu Ile Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala
          130                 135                 140

      GAC ATA ATT CAC AGG GAC CTA AAA CCT AGT AAT CTA GCT GTG AAT GAA     480
   5  Asp Ile Ile His Arg Asp Leu Lys Pro Ser Asn Leu Ala Val Asn Glu
          145                 150                 155                 160

      GAC TGT GAG CTG AAG ATT CTG GAT TTT GGA CTG GCT CGG CAC ACA GAT     528
      Asp Cys Glu Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg His Thr Asp
  10                      165                 170                 175

      GAT GAA ATG ACA GGC TAC GTG GCC ACT AGG TGG TAC AGG GCT CCT GAG     576
      Asp Glu Met Thr Gly Tyr Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu
                      180                 185                 190
  15

      ATC ATG CTG AAC TGG ATG CAT TAC AAC CAG ACA GTT GAT ATT TGG TCA     624
      Ile Met Leu Asn Trp Met His Tyr Asn Gln Thr Val Asp Ile Trp Ser
                  195                 200                 205

  20  GTG GGA TGC ATA ATG GCC GAG CTG TTG ACT GGA AGA ACA TTG TTT CCT     672
      Val Gly Cys Ile Met Ala Glu Leu Leu Thr Gly Arg Thr Leu Phe Pro
                  210                 215                 220

      GGT ACA GAC CAT ATT GAT CAG TTG AAG CTC ATT TTA AGA CTC GTT GGA     720
  25  Gly Thr Asp His Ile Asp Gln Leu Lys Leu Ile Leu Arg Leu Val Gly
          225                 230                 235                 240

      ACC CCA GGG GCT GAG CTT TTG AAG AAA ATC TCC TCA GAG TCT GCA AGA     768
      Thr Pro Gly Ala Glu Leu Leu Lys Lys Ile Ser Ser Glu Ser Ala Arg
  30                  245                 250                 255

      AAC TAT ATT CAG TCT TTG ACT CAG ATG CCG AAG ATG AAC TTT GCG AAT     816
      Asn Tyr Ile Gln Ser Leu Thr Gln Met Pro Lys Met Asn Phe Ala Asn
                      260                 265                 270
  35
      GTA TTT ATT GGT GCC AAT CCC CTG GCT GTC GAC TTG CTG GAG AAG ATG     864
      Val Phe Ile Gly Ala Asn Pro Leu Ala Val Asp Leu Leu Glu Lys Met
                  275                 280                 285

  40  CTT GTA TTG GAC TCA GAT AAG AGA ATT ACA GCG GCC CAA GCC CTT GCA     912
      Leu Val Leu Asp Ser Asp Lys Arg Ile Thr Ala Ala Gln Ala Leu Ala
                  290                 295                 300

      CAT GCC TAC TTT GCT CAG TAC CAC GAT CCT GAT GAT GAA CCA GTG GCC     960
  45  His Ala Tyr Phe Ala Gln Tyr His Asp Pro Asp Asp Glu Pro Val Ala
          305                 310                 315                 320

      GAT CCT TAT GAT CAG TCC TTT GAA AGC AGG GAC CTC CTT ATA GAT GAG    1008
      Asp Pro Tyr Asp Gln Ser Phe Glu Ser Arg Asp Leu Leu Ile Asp Glu
  50                      325                 330                 335

      TGG AAA AGC CTG ACC TAT GAT GAA GTC ATC AGC TTT GTG CCA CCA CCC    1056
      Trp Lys Ser Leu Thr Tyr Asp Glu Val Ile Ser Phe Val Pro Pro Pro
                      340                 345                 350
  55
      CTT GAC CAA GAA GAG ATG GAG TCC GAG GAT CCA CCG GTC GCC ACC ATG    1104
```

140

```
        Leu Asp Gln Glu Glu Met Glu Ser Glu Asp Pro Pro Val Ala Thr Met
                355             360             365

 5      GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC   1152
        Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                370             375             380

        GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG   1200
10      Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
        385             390             395             400

        GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC   1248
        Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
                        405             410             415
15

        ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG   1296
        Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
                        420             425             430

20      ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG   1344
        Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
                        435             440             445

        CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC   1392
25      His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                450             455             460

        ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG   1440
        Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
30      465             470             475             480

        AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC   1488
        Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
                        485             490             495
35

        GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC   1536
        Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
                        500             505             510

40      TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC   1584
        Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
                515             520             525

        ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG   1632
45      Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
                530             535             540

        CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC   1680
        Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
50      545             550             555             560

        GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC   1728
        Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
                        565             570             575
55

        AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG   1776
```

140

SUBSTITUTE SHEET (RULE 26)

```
      Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
              580                     585                 590

      ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA        1821
  5   Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
              595                     600                 605
```

 10   (2) INFORMATION FOR SEQ ID NO:65:

             (i) SEQUENCE CHARACTERISTICS:
                 (A) LENGTH: 606 amino acids
                 (B) TYPE: amino acid
                 (C) STRANDEDNESS: single
 15   (D) TOPOLOGY: linear

             (ii) MOLECULE TYPE: protein
             (v) FRAGMENT TYPE: internal

 20   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

```
      Met Ser Gln Glu Arg Pro Thr Phe Tyr Arg Gln Glu Leu Asn Lys Thr
        1               5                  10              15
      Ile Trp Glu Val Pro Glu Arg Tyr Gln Asn Leu Ser Pro Val Gly Ser
 25               20                  25                  30
      Gly Ala Tyr Gly Ser Val Cys Ala Ala Phe Asp Thr Lys Thr Gly Leu
                  35                  40                  45
      Arg Val Ala Val Lys Lys Leu Ser Arg Pro Phe Gln Ser Ile Ile His
               50                  55                  60
 30   Ala Lys Arg Thr Tyr Arg Glu Leu Arg Leu Leu Lys His Met Lys His
       65                  70                  75                  80
      Glu Asn Val Ile Gly Leu Leu Asp Val Phe Thr Pro Ala Arg Ser Leu
                  85                  90                  95
      Glu Glu Phe Asn Asp Val Tyr Leu Val Thr His Leu Met Gly Ala Asp
 35              100                 105                 110
      Leu Asn Asn Ile Val Lys Cys Gln Lys Leu Thr Asp Asp His Val Gln
                  115                 120                 125
      Phe Leu Ile Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala
                  130                 135                 140
 40   Asp Ile Ile His Arg Asp Leu Lys Pro Ser Asn Leu Ala Val Asn Glu
          145                 150                 155                 160
      Asp Cys Glu Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg His Thr Asp
                  165                 170                 175
      Asp Glu Met Thr Gly Tyr Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu
 45              180                 185                 190
      Ile Met Leu Asn Trp Met His Tyr Asn Gln Thr Val Asp Ile Trp Ser
                  195                 200                 205
      Val Gly Cys Ile Met Ala Glu Leu Leu Thr Gly Arg Thr Leu Phe Pro
                  210                 215                 220
 50   Gly Thr Asp His Ile Asp Gln Leu Lys Leu Ile Leu Arg Leu Val Gly
          225                 230                 235                 240
      Thr Pro Gly Ala Glu Leu Leu Lys Lys Ile Ser Ser Glu Ser Ala Arg
                  245                 250                 255
      Asn Tyr Ile Gln Ser Leu Thr Gln Met Pro Lys Met Asn Phe Ala Asn
 55               260                 265                 270
      Val Phe Ile Gly Ala Asn Pro Leu Ala Val Asp Leu Leu Glu Lys Met
```

```
             275                  280                  285
      Leu Val Leu Asp Ser Asp Lys Arg Ile Thr Ala Ala Gln Ala Leu Ala
          290                  295                  300
      His Ala Tyr Phe Ala Gln Tyr His Asp Pro Asp Asp Glu Pro Val Ala
 5    305                  310                  315                  320
      Asp Pro Tyr Asp Gln Ser Phe Glu Ser Arg Asp Leu Leu Ile Asp Glu
                       325                  330                  335
      Trp Lys Ser Leu Thr Tyr Asp Glu Val Ile Ser Phe Val Pro Pro Pro
                   340                  345                  350
10    Leu Asp Gln Glu Glu Met Glu Ser Glu Asp Pro Pro Val Ala Thr Met
                   355                  360                  365
      Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
          370                  375                  380
      Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
15    385                  390                  395                  400
      Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
                       405                  410                  415
      Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
                   420                  425                  430
20    Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
                   435                  440                  445
      His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                   450                  455                  460
      Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
25    465                  470                  475                  480
      Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
                       485                  490                  495
      Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
                   500                  505                  510
30    Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
                   515                  520                  525
      Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
                   530                  535                  540
      Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
35    545                  550                  555                  560
      Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
                   565                  570                  575
      Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
                   580                  585                  590
40    Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
          595                  600                  605
```

                (2) INFORMATION FOR SEQ ID NO:66:

45   (i) SEQUENCE CHARACTERISTICS:
                   (A) LENGTH: 2913 base pairs
                   (B) TYPE: nucleic acid
                   (C) STRANDEDNESS: single
                   (D) TOPOLOGY: linear
50
                (ii) MOLECULE TYPE: cDNA
                (ix) FEATURE:

                   (A) NAME/KEY: Coding Sequence
55   (B) LOCATION: 1...2910
                   (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

```
       ATG AGT GCT GAG GGG TAC CAG TAC AGA GCG CTG TAT GAT TAT AAA AAG       ~48
  5    Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys
        1               5                  10                 15

       GAA AGA GAA GAA GAT ATT GAC TTG CAC TTG GGT GAC ATA TTG ACT GTG        96
       Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp Ile Leu Thr Val
 10                     20                 25                 30

       AAT AAA GGG TCC TTA GTA GCT CTT GGA TTC AGT GAT GGA CAG GAA GCC       144
       Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp Gly Gln Glu Ala
                   35                  40                 45
 15
       AGG CCT GAA GAA ATT GGC TGG TTA AAT GGC TAT AAT GAA ACC ACA GGG       192
       Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn Glu Thr Thr Gly
           50                  55                 60

 20    GAA AGG GGG GAC TTT CCG GGA ACT TAC GTA GAA TAT ATT GGA AGG AAA       240
       Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr Ile Gly Arg Lys
       65                  70                 75                 80

       AAA ATC TCG CCT CCC ACA CCA AAG CCC CGG CCA CCT CGG CCT CTT CCT       288
 25    Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro Arg Pro Leu Pro
                       85                  90                 95

       GTT GCA CCA GGT TCT TCG AAA ACT GAA GCA GAT GTT GAA CAA CAA GCT       336
       Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val Glu Gln Gln Ala
 30                    100                105                110

       TTG ACT CTC CCG GAT CTT GCA GAG CAG TTT GCC CCT CCT GAC ATT GCC       384
       Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro Pro Asp Ile Ala
                  115                 120                125
 35
       CCG CCT CTT CTT ATC AAG CTC GTG GAA GCC ATT GAA AAG AAA GGT CTG       432
       Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu Lys Lys Gly Leu
           130                 135                140

 40    GAA TGT TCA ACT CTA TAC AGA ACA CAG AGC TCC AGC AAC CTG GCA GAA       480
       Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser Asn Leu Ala Glu
       145                 150                155                160

       TTA CGA CAG CTT CTT GAT TGT GAT ACA CCC TCC GTG GAC TTG GAA ATG       528
 45    Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val Asp Leu Glu Met
                       165                170                175

       ATC GAT GTG CAC GTT TTG GCT GAC GCT TTC AAA CGC TAT CTC CTG GAC       576
       Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg Tyr Leu Leu Asp
 50                    180                185                190

       TTA CCA AAT CCT GTC ATT CCA GCA GCC GTT TAC AGT GAA ATG ATT TCT       624
       Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser Glu Met Ile Ser
                   195                 200                205
 55
       TTA GCT CCA GAA GTA CAA AGC TCC GAA GAA TAT ATT CAG CTA TTG AAG       672
```

143

144

```
      Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile Gln Leu Leu Lys
          210             215             220

 5    AAG CTT ATT AGG TCG CCT AGC ATA CCT CAT CAG TAT TGG CTT ACG CTT        720
      Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr Trp Leu Thr Leu
      225             230             235             240

      CAG TAT TTG TTA AAA CAT TTC TTC AAG CTC TCT CAA ACC TCC AGC AAA        768
      Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln Thr Ser Ser Lys
10                245             250             255

      AAT CTG TTG AAT GCA AGA GTA CTC TCT GAA ATT TTC AGC CCT ATG CTT        816
      Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe Ser Pro Met Leu
                  260             265             270
15
      TTC AGA TTC TCA GCA GCC AGC TCT GAT AAT ACT GAA AAC CTC ATA AAA        864
      Phe Arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu Asn Leu Ile Lys
              275             280             285

20    GTT ATA GAA ATT TTA ATC TCA ACT GAA TGG AAT GAA CGA CAG CCT GCA        912
      Val Ile Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu Arg Gln Pro Ala
              290             295             300

      CCA GCA CTG CCT CCT AAA CCA CCA AAA CCT ACT ACT GTA GCC AAC AAC        960
25    Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr Val Ala Asn Asn
      305             310             315             320

      GGT ATG AAT AAC AAT ATG TCC TTA CAA AAT GCT GAA TGG TAC TGG GGA       1008
      Gly Met Asn Asn Asn Met Ser Leu Gln Asn Ala Glu Trp Tyr Trp Gly
30                325             330             335

      GAT ATC TCG AGG GAA GAA GTG AAT GAA AAA CTT CGA GAT ACA GCA GAC       1056
      Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg Asp Thr Ala Asp
              340             345             350
35
      GGG ACC TTT TTG GTA CGA GAT GCG TCT ACT AAA ATG CAT GGT GAT TAT       1104
      Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met His Gly Asp Tyr
              355             360             365

40    ACT CTT ACA CTA AGG AAA GGG GGA AAT AAC AAA TTA ATC AAA ATA TTT       1152
      Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu Ile Lys Ile Phe
              370             375             380

      CAT CGA GAT GGG AAA TAT GGC TTC TCT GAC CCA TTA ACC TTC AGT TCT       1200
45    His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu Thr Phe Ser Ser
      385             390             395             400

      GTG GTT GAA TTA ATA AAC CAC TAC CGG AAT GAA TCT CTA GCT CAG TAT       1248
      Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser Leu Ala Gln Tyr
50                405             410             415

      AAT CCC AAA TTG GAT GTG AAA TTA CTT TAT CCA GTA TCC AAA TAC CAA       1296
      Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val Ser Lys Tyr Gln
                  420             425             430
55
      CAG GAT CAA GTT GTC AAA GAA GAT AAT ATT GAA GCT GTA GGG AAA AAA       1344
```

144

145

```
           Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala Val Gly Lys Lys
                   435             440             445

  5        TTA CAT GAA TAT AAC ACT CAG TTT CAA GAA AAA AGT CGA GAA TAT GAT    1392
           Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser Arg Glu Tyr Asp
                   450             455             460

           AGA TTA TAT GAA GAA TAT ACC CGC ACA TCC CAG GAA ATC CAA ATG AAA    1440
           Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu Ile Gln Met Lys
 10        465             470             475             480

           AGG ACA GCT ATT GAA GCA TTT AAT GAA ACC ATA AAA ATA TTT GAA GAA    1488
           Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys Ile Phe Glu Glu
                           485             490             495
 15
           CAG TGC CAG ACC CAA GAG CGG TAC AGC AAA GAA TAC ATA GAA AAG TTT    1536
           Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr Ile Glu Lys Phe
                       500             505             510

 20        AAA CGT GAA GGC AAT GAG AAA GAA ATA CAA AGG ATT ATG CAT AAT TAT    1584
           Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile Met His Asn Tyr
                       515             520             525

           GAT AAG TTG AAG TCT CGA ATC AGT GAA ATT ATT GAC AGT AGA AGA AGA    1632
 25        Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp Ser Arg Arg Arg
                   530             535             540

           TTG GAA GAA GAC TTG AAG AAG CAG GCA GCT GAG TAT CGA GAA ATT GAC    1680
           Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr Arg Glu Ile Asp
 30        545             550             555             560

           AAA CGT ATG AAC AGC ATT AAA CCA GAC CTT ATC CAG CTG AGA AAG ACG    1728
           Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln Leu Arg Lys Thr
                       565             570             575
 35
           AGA GAC CAA TAC TTG ATG TGG TTG ACT CAA AAA GGT GTT CGG CAA AAG    1776
           Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly Val Arg Gln Lys
                       580             585             590

 40        AAG TTG AAC GAG TGG TTG GGC AAT GAA AAC ACT GAA GAC CAA TAT TCA    1824
           Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu Asp Gln Tyr Ser
                   595             600             605

           CTG GTG GAA GAT GAT GAA GAT TTG CCC CAT CAT GAT GAG AAG ACA TGG    1872
 45        Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp Glu Lys Thr Trp
                   610             615             620

           AAT GTT GGA AGC AGC AAC CGA AAC AAA GCT GAA AAC CTG TTG CGA GGG    1920
           Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn Leu Leu Arg Gly
 50        625             630             635             640

           AAG CGA GAT GGC ACT TTT CTT GTC CGG GAG AGC AGT AAA CAG GGC TGC    1968
           Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser Lys Gln Gly Cys
                           645             650             655
 55
           TAT GCC TGC TCT GTA GTG GTG GAC GGC GAA GTA AAG CAT TGT GTC ATA    2016
```

145

146

```
          Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys His Cys Val Ile
                      660                 665                 670

  5       AAC AAA ACA GCA ACT GGC TAT GGC TTT GCC GAG CCC TAT AAC TTG TAC        2064
          Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro Tyr Asn Leu Tyr
                      675                 680                 685

          AGC TCT CTG AAA GAA CTG GTG CTA CAT TAC CAA CAC ACC TCC CTT GTG        2112
 10       Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His Thr Ser Leu Val
                  690                 695                 700

          CAG CAC AAC GAC TCC CTC AAT GTC ACA CTA GCC TAC CCA GTA TAT GCA        2160
          Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr Pro Val Tyr Ala
          705                 710                 715                 720
 15
          CAG CAG AGG CGA CAG GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC        2208
          Gln Gln Arg Arg Gln Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly
                          725                 730                 735

 20       GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC        2256
          Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly
                      740                 745                 750

          GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT        2304
 25       Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp
                      755                 760                 765

          GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG        2352
          Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys
 30            770                 775                 780

          CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG        2400
          Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val
          785                 790                 795                 800
 35
          CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC        2448
          Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe
                          805                 810                 815

 40       AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC        2496
          Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe
                          820                 825                 830

          AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC        2544
 45       Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly
                      835                 840                 845

          GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG        2592
          Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu
 50           850                 855                 860

          GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC        2640
          Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His
          865                 870                 875                 880
 55
          AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC        2688
```

BNSDOCID: <WO___9845704A2_I_>

```
    Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn
                    885                 890                 895
```

```
 5  TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC    2736
    Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp
                    900                 905                 910
```

```
    CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC    2784
10  His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro
                    915                 920                 925
```

```
    GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC    2832
    Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn
                    930                 935                 940
15
    GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG    2880
    Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly
    945                 950                 955                 960
```

```
20  ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA                        2913
    Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
                    965                 970
```


```
25          (2) INFORMATION FOR SEQ ID NO:67:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 970 amino acids
            (B) TYPE: amino acid
30          (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein
        (v) FRAGMENT TYPE: internal
35
        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:
```

```
    Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys
    1               5                   10                  15
40  Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp Ile Leu Thr Val
                    20                  25                  30
    Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp Gly Gln Glu Ala
                35                  40                  45
    Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn Glu Thr Thr Gly
45          50                  55                  60
    Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr Ile Gly Arg Lys
    65              70                  75                  80
    Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Arg Pro Leu Pro
                    85                  90                  95
50  Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val Glu Gln Gln Ala
                    100                 105                 110
    Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro Pro Asp Ile Ala
                115                 120                 125
    Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu Lys Lys Gly Leu
55          130                 135                 140
    Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser Asn Leu Ala Glu
```

BNSDOCID: <WO___9845704A2_I_>

```
      145               150               155               160
      Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val Asp Leu Glu Met
                  165               170               175
      Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg Tyr Leu Leu Asp
  5               180               185               190
      Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser Glu Met Ile Ser
                  195               200               205
      Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile Gln Leu Leu Lys
                  210               215               220
 10   Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr Trp Leu Thr Leu
      225               230               235               240
      Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln Thr Ser Ser Lys
                  245               250               255
      Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe Ser Pro Met Leu
 15               260               265               270
      Phe Arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu Asn Leu Ile Lys
                  275               280               285
      Val Ile Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu Arg Gln Pro Ala
                  290               295               300
 20   Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr Val Ala Asn Asn
      305               310               315               320
      Gly Met Asn Asn Asn Met Ser Leu Gln Asn Ala Glu Trp Tyr Trp Gly
                  325               330               335
      Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg Asp Thr Ala Asp
 25               340               345               350
      Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met His Gly Asp Tyr
                  355               360               365
      Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu Ile Lys Ile Phe
                  370               375               380
 30   His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu Thr Phe Ser Ser
      385               390               395               400
      Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser Leu Ala Gln Tyr
                  405               410               415
      Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val Ser Lys Tyr Gln
 35               420               425               430
      Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala Val Gly Lys Lys
                  435               440               445
      Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser Arg Glu Tyr Asp
                  450               455               460
 40   Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu Ile Gln Met Lys
      465               470               475               480
      Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys Ile Phe Glu Glu
                  485               490               495
      Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr Ile Glu Lys Phe
 45               500               505               510
      Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile Met His Asn Tyr
                  515               520               525
      Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp Ser Arg Arg Arg
                  530               535               540
 50   Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr Arg Glu Ile Asp
      545               550               555               560
      Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln Leu Arg Lys Thr
                  565               570               575
      Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly Val Arg Gln Lys
 55               580               585               590
      Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu Asp Gln Tyr Ser
```

```
              595                  600                  605
    Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp Glu Lys Thr Trp
        610                  615                  620
    Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn Leu Leu Arg Gly
5   625                  630                  635                  640
    Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser Lys Gln Gly Cys
                    645                  650                  655
    Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys His Cys Val Ile
                    660                  665                  670
10  Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro Tyr Asn Leu Tyr
                    675                  680                  685
    Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His Thr Ser Leu Val
        690                  695                  700
    Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr Pro Val Tyr Ala
15  705                  710                  715                  720
    Gln Gln Arg Arg Gln Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly
                    725                  730                  735
    Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly
                    740                  745                  750
20  Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp
        755                  760                  765
    Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys
        770                  775                  780
    Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val
25  785                  790                  795                  800
    Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe
                    805                  810                  815
    Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe
                    820                  825                  830
30  Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly
        835                  840                  845
    Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu
        850                  855                  860
    Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His
35  865                  870                  875                  880
    Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn
                    885                  890                  895
    Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp
                    900                  905                  910
40  His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro
        915                  920                  925
    Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn
        930                  935                  940
    Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly
45  945                  950                  955                  960
    Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
                    965                  970
```

        (2) INFORMATION FOR SEQ ID NO:68:

50
            (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 1788 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
55   (D) TOPOLOGY: linear

```
(ii)  MOLECULE TYPE: cDNA
(ix)  FEATURE:

      (A)  NAME/KEY: Coding Sequence
      (B)  LOCATION: 1...1785
      (D)  OTHER INFORMATION:

(xi)  SEQUENCE DESCRIPTION: SEQ ID NO:68:
```

```
ATG GGC AAC GCC GCC GCC GCC AAG AAG GGC AGC GAG CAG GAG AGC GTG        48
Met Gly Asn Ala Ala Ala Ala Lys Lys Gly Ser Glu Gln Glu Ser Val
 1               5                  10                  15

AAA GAG TTC CTA GCC AAA GCC AAG GAA GAT TTC CTG AAA AAA TGG GAA        96
Lys Glu Phe Leu Ala Lys Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu
            20                  25                  30

GAC CCC TCT CAG AAT ACA GCC CAG TTG GAT CAG TTT GAT AGA ATC AAG       144
Asp Pro Ser Gln Asn Thr Ala Gln Leu Asp Gln Phe Asp Arg Ile Lys
            35                  40                  45

ACC CTT GGC ACC GGC TCC TTT GGG CGA GTG ATG CTG GTG AAG CAC AAG       192
Thr Leu Gly Thr Gly Ser Phe Gly Arg Val Met Leu Val Lys His Lys
        50                  55                  60

GAG AGT GGG AAC CAC TAC GCC ATG AAG ATC TTA GAC AAG CAG AAG GTG       240
Glu Ser Gly Asn His Tyr Ala Met Lys Ile Leu Asp Lys Gln Lys Val
65                  70                  75                  80

GTG AAG CTA AAG CAG ATC GAG CAC ACT CTG AAT GAG AAG CGC ATC CTG       288
Val Lys Leu Lys Gln Ile Glu His Thr Leu Asn Glu Lys Arg Ile Leu
                85                  90                  95

CAG GCC GTC AAC TTC CCG TTC CTG GTC AAA CTT GAA TTC TCC TTC AAG       336
Gln Ala Val Asn Phe Pro Phe Leu Val Lys Leu Glu Phe Ser Phe Lys
            100                 105                 110

GAC AAC TCA AAC CTG TAC ATG GTC ATG GAG TAT GTA GCT GGT GGC GAG       384
Asp Asn Ser Asn Leu Tyr Met Val Met Glu Tyr Val Ala Gly Gly Glu
            115                 120                 125

ATG TTC TCC CAC CTA CGG CGG ATT GGA AGG TTC AGC GAG CCC CAT GCC       432
Met Phe Ser His Leu Arg Arg Ile Gly Arg Phe Ser Glu Pro His Ala
            130                 135                 140

CGT TTC TAC GCG GCG CAG ATC GTC CTG ACC TTT GAG TAT CTG CAC TCC       480
Arg Phe Tyr Ala Ala Gln Ile Val Leu Thr Phe Glu Tyr Leu His Ser
145                 150                 155                 160

CTG GAC CTC ATC TAC CGG GAC CTG AAG CCC GAG AAT CTT CTC ATC GAC       528
Leu Asp Leu Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp
                165                 170                 175

CAG CAG GGC TAT ATT CAG GTG ACA GAC TTC GGT TTT GCC AAG CGT GTG       576
Gln Gln Gly Tyr Ile Gln Val Thr Asp Phe Gly Phe Ala Lys Arg Val
            180                 185                 190
```

```
   AAA GGC CGT ACT TGG ACC TTG TGT GGG ACC CCT GAG TAC TTG GCC CCC    624
   Lys Gly Arg Thr Trp Thr Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro
           195                     200                 205
5
   GAG ATT ATC CTG AGC AAA GGC TAC AAC AAG GCT GTG GAC TGG TGG GCT    672
   Glu Ile Ile Leu Ser Lys Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala
           210                     215                 220
10 CTC GGA GTC CTC ATC TAC GAG ATG GCT GCT GGT TAC CCA CCC TTC TTC    720
   Leu Gly Val Leu Ile Tyr Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe
   225                     230                 235                 240
   GCT GAC CAG CCT ATC CAG ATC TAT GAG AAA ATC GTC TCT GGG AAG GTG    768
15 Ala Asp Gln Pro Ile Gln Ile Tyr Glu Lys Ile Val Ser Gly Lys Val
                       245                 250                 255
   CGG TTC CCA TCC CAC TTC AGC TCT GAC TTG AAG GAC CTG CTG CGG AAC    816
   Arg Phe Pro Ser His Phe Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn
20                 260                 265                 270
   CTT CTG CAA GTG GAT CTA ACC AAG CGC TTT GGA AAC CTC AAG GAC GGG    864
   Leu Leu Gln Val Asp Leu Thr Lys Arg Phe Gly Asn Leu Lys Asp Gly
                   275                 280                 285
25
   GTC AAT GAC ATC AAG AAC CAC AAG TGG TTT GCC ACG ACT GAC TGG ATT    912
   Val Asn Asp Ile Lys Asn His Lys Trp Phe Ala Thr Thr Asp Trp Ile
           290                 295                 300
30 GCC ATC TAT CAG AGA AAG GTG GAA GCT CCC TTC ATA CCA AAG TTT AAA    960
   Ala Ile Tyr Gln Arg Lys Val Glu Ala Pro Phe Ile Pro Lys Phe Lys
   305                 310                 315                 320
   GGC CCT GGG GAC ACG AGT AAC TTT GAC GAC TAT GAG GAG GAA GAG ATC   1008
35 Gly Pro Gly Asp Thr Ser Asn Phe Asp Asp Tyr Glu Glu Glu Glu Ile
                   325                 330                 335
   CGG GTC TCC ATC AAT GAG AAG TGT GGC AAG GAG TTT ACT GAG TTT GGG   1056
   Arg Val Ser Ile Asn Glu Lys Cys Gly Lys Glu Phe Thr Glu Phe Gly
40                 340                 345                 350
   CGC GCC ATG AGT AAA GGA GAA GAA CTT TTC ACT GGA GTT GTC CCA ATT   1104
   Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile
                   355                 360                 365
45
   CTT GTT GAA TTA GAT GGC GAT GTT AAT GGG CAA AAA TTC TCT GTT AGT   1152
   Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser
           370                 375                 380
50 GGA GAG GGT GAA GGT GAT GCA ACA TAC GGA AAA CTT ACC CTT AAA TTT   1200
   Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe
   385                 390                 395                 400
   ATT TGC ACT ACT GGG AAG CTA CCT GTT CCA TGG CCA ACG CTT GTC ACT   1248
55 Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
                   405                 410                 415
```

```
ACT CTC ACT TAT GGT GTT CAA TGC TTT TCT AGA TAC CCA GAT CAT ATG      1296
Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
            420                 425                 430

AAA CAG CAT GAC TTT TTC AAG AGT GCC ATG CCC GAA GGT TAT GTA CAG      1344
Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
            435                 440                 445

GAA AGA ACT ATA TTT TAC AAA GAT GAC GGG AAC TAC AAG ACA CGT GCT      1392
Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
            450                 455                 460

GAA GTC AAG TTT GAA GGT GAT ACC CTT GTT AAT AGA ATC GAG TTA AAA      1440
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
465                 470                 475                 480

GGT ATT GAT TTT AAA GAA GAT GGA AAC ATT CTT GGA CAC AAA ATG GAA      1488
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu
                485                 490                 495

TAC AAT TAT AAC TCA CAT AAT GTA TAC ATC ATG GCA GAC AAA CCA AAG      1536
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys
            500                 505                 510

AAT GGC ATC AAA GTT AAC TTC AAA ATT AGA CAC AAC ATT AAA GAT GGA      1584
Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly
            515                 520                 525

AGC GTT CAA TTA GCA GAC CAT TAT CAA CAA AAT ACT CCA ATT GGC GAT      1632
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
            530                 535                 540

GGC CCT GTC CTT TTA CCA GAC AAC CAT TAC CTG TCC ACG CAA TCT GCC      1680
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
545                 550                 555                 560

CTT TCC AAA GAT CCC AAC GAA AAG AGA GAT CAC ATG ATC CTT CTT GAG      1728
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu
                565                 570                 575

TTT GTA ACA GCT GCT GGG ATT ACA CAT GGC ATG GAT GAA CTA TAC AAA      1776
Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys
            580                 585                 590

CCT CAG GAG TAA                                                      1788
Pro Gln Glu
        595
```

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 595 amino acids
    (B) TYPE: amino acid
    (C) STRANDEDNESS: single

        (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein
        (v) FRAGMENT TYPE: internal

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

    Met Gly Asn Ala Ala Ala Ala Lys Lys Gly Ser Glu Gln Glu Ser Val
    1   5   10   15
    Lys Glu Phe Leu Ala Lys Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu
                    20   25   30
    Asp Pro Ser Gln Asn Thr Ala Gln Leu Asp Gln Phe Asp Arg Ile Lys
                35   40   45
    Thr Leu Gly Thr Gly Ser Phe Gly Arg Val Met Leu Val Lys His Lys
    50   55   60
    Glu Ser Gly Asn His Tyr Ala Met Lys Ile Leu Asp Lys Gln Lys Val
    65   70   75   80
    Val Lys Leu Lys Gln Ile Glu His Thr Leu Asn Glu Lys Arg Ile Leu
                    85   90   95
    Gln Ala Val Asn Phe Pro Phe Leu Val Lys Leu Glu Phe Ser Phe Lys
                    100   105   110
    Asp Asn Ser Asn Leu Tyr Met Val Met Glu Tyr Val Ala Gly Gly Glu
                115   120   125
    Met Phe Ser His Leu Arg Arg Ile Gly Arg Phe Ser Glu Pro His Ala
    130   135   140
    Arg Phe Tyr Ala Ala Gln Ile Val Leu Thr Phe Glu Tyr Leu His Ser
    145   150   155   160
    Leu Asp Leu Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp
                    165   170   175
    Gln Gln Gly Tyr Ile Gln Val Thr Asp Phe Gly Phe Ala Lys Arg Val
                    180   185   190
    Lys Gly Arg Thr Trp Thr Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro
                    195   200   205
    Glu Ile Ile Leu Ser Lys Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala
    210   215   220
    Leu Gly Val Leu Ile Tyr Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe
    225   230   235   240
    Ala Asp Gln Pro Ile Gln Ile Tyr Glu Lys Ile Val Ser Gly Lys Val
                    245   250   255
    Arg Phe Pro Ser His Phe Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn
                    260   265   270
    Leu Leu Gln Val Asp Leu Thr Lys Arg Phe Gly Asn Leu Lys Asp Gly
                    275   280   285
    Val Asn Asp Ile Lys Asn His Lys Trp Phe Ala Thr Thr Asp Trp Ile
    290   295   300
    Ala Ile Tyr Gln Arg Lys Val Glu Ala Pro Phe Ile Pro Lys Phe Lys
    305   310   315   320
    Gly Pro Gly Asp Thr Ser Asn Phe Asp Asp Tyr Glu Glu Glu Glu Ile
                    325   330   335
    Arg Val Ser Ile Asn Glu Lys Cys Gly Lys Glu Phe Thr Glu Phe Gly
                    340   345   350
    Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile
                    355   360   365
    Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser
    370   375   380
    Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe

```
385                        390                        395                        400
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
                    405                        410                        415
Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
             420                        425                        430
Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
             435                        440                        445
Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
       450                        455                        460
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
465                        470                        475                        480
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu
                    485                        490                        495
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys
             500                        505                        510
Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly
             515                        520                        525
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
       530                        535                        540
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
545                        550                        555                        560
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu
                    565                        570                        575
Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys
                    580                        585                        590
Pro Gln Glu
       595
```

        (2) INFORMATION FOR SEQ ID NO:70:

        (i) SEQUENCE CHARACTERISTICS:
           (A) LENGTH: 2181 base pairs
           (B) TYPE: nucleic acid
           (C) STRANDEDNESS: single
           (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: cDNA
        (ix) FEATURE:

           (A) NAME/KEY: Coding Sequence
           (B) LOCATION: 1...2178
           (D) OTHER INFORMATION:

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

```
ATG AGC GAC GTG GCT ATT GTG AAG GAG GGT TGG CTG CAC AAA CGA GGG        48
Met Ser Asp Val Ala Ile Val Lys Glu Gly Trp Leu His Lys Arg Gly
 1                   5                        10                        15

GAG TAC ATC AAG ACC TGG CGG CCA CGC TAC TTC CTC CTC AAG AAT GAT        96
Glu Tyr Ile Lys Thr Trp Arg Pro Arg Tyr Phe Leu Leu Lys Asn Asp
                    20                        25                        30

GGC ACC TTC ATT GGC TAC AAG GAG CGG CCG CAG GAT GTG GAC CAA CGT       144
Gly Thr Phe Ile Gly Tyr Lys Glu Arg Pro Gln Asp Val Asp Gln Arg
             35                        40                        45
```

```
        GAG GCT CCC CTC AAC AAC TTC TCT GTG GCG CAG TGC CAG CTG ATG AAG      192
        Glu Ala Pro Leu Asn Asn Phe Ser Val Ala Gln Cys Gln Leu Met Lys
            50              55              60
  5
        ACG GAG CGG CCC CGG CCC AAC ACC TTC ATC ATC CGC TGC CTG CAG TGG      240
        Thr Glu Arg Pro Arg Pro Asn Thr Phe Ile Ile Arg Cys Leu Gln Trp
        65              70              75              80

 10     ACC ACT GTC ATC GAA CGC ACC TTC CAT GTG GAG ACT CCT GAG GAG CGG      288
        Thr Thr Val Ile Glu Arg Thr Phe His Val Glu Thr Pro Glu Glu Arg
                        85              90              95

        GAG GAG TGG ACA ACC GCC ATC CAG ACT GTG GCT GAC GGC CTC AAG AAG      336
 15     Glu Glu Trp Thr Thr Ala Ile Gln Thr Val Ala Asp Gly Leu Lys Lys
                    100             105             110

        CAG GAG GAG GAG GAG ATG GAC TTC CGG TCG GGC TCA CCC AGT GAC AAC      384
        Gln Glu Glu Glu Glu Met Asp Phe Arg Ser Gly Ser Pro Ser Asp Asn
 20             115             120             125

        TCA GGG GCT GAA GAG ATG GAG GTG TCC CTG GCC AAG CCC AAG CAC CGC      432
        Ser Gly Ala Glu Glu Met Glu Val Ser Leu Ala Lys Pro Lys His Arg
            130             135             140
 25
        GTG ACC ATG AAC GAG TTT GAG TAC CTG AAG CTG CTG GGC AAG GGC ACT      480
        Val Thr Met Asn Glu Phe Glu Tyr Leu Lys Leu Leu Gly Lys Gly Thr
        145             150             155             160

 30     TTC GGC AAG GTG ATC CTG GTG AAG GAG AAG GCC ACA GGC CGC TAC TAC      528
        Phe Gly Lys Val Ile Leu Val Lys Glu Lys Ala Thr Gly Arg Tyr Tyr
                        165             170             175

        GCC ATG AAG ATC CTC AAG AAG GAA GTC ATC GTG GCC AAG GAC GAG GTG      576
 35     Ala Met Lys Ile Leu Lys Lys Glu Val Ile Val Ala Lys Asp Glu Val
                    180             185             190

        GCC CAC ACA CTC ACC GAG AAC CGC GTC CTG CAG AAC TCC AGG CAC CCC      624
        Ala His Thr Leu Thr Glu Asn Arg Val Leu Gln Asn Ser Arg His Pro
 40             195             200             205

        TTC CTC ACA GCC CTG AAG TAC TCT TTC CAG ACC CAC GAC CGC CTC TGC      672
        Phe Leu Thr Ala Leu Lys Tyr Ser Phe Gln Thr His Asp Arg Leu Cys
            210             215             220
 45
        TTT GTC ATG GAG TAC GCC AAC GGG GGC GAG CTG TTC TTC CAC CTG TCC      720
        Phe Val Met Glu Tyr Ala Asn Gly Gly Glu Leu Phe Phe His Leu Ser
        225             230             235             240

 50     CGG GAA CGT GTG TTC TCC GAG GAC CGG GCC CGC TTC TAT GGC GCT GAG      768
        Arg Glu Arg Val Phe Ser Glu Asp Arg Ala Arg Phe Tyr Gly Ala Glu
                        245             250             255

        ATT GTG TCA GCC CTG GAC TAC CTG CAC TCG GAG AAG AAC GTG GTG TAC      816
 55     Ile Val Ser Ala Leu Asp Tyr Leu His Ser Glu Lys Asn Val Val Tyr
                    260             265             270
```

155

```
CGG GAC CTC AAG CTG GAG AAC CTC ATG CTG GAC AAG GAC GGG CAC ATT        864
Arg Asp Leu Lys Leu Glu Asn Leu Met Leu Asp Lys Asp Gly His Ile
        275             280             285

AAG ATC ACA GAC TTC GGG CTG TGC AAG GAG GGG ATC AAG GAC GGT GCC        912
Lys Ile Thr Asp Phe Gly Leu Cys Lys Glu Gly Ile Lys Asp Gly Ala
        290             295             300

ACC ATG AAG ACC TTT TGC GGC ACA CCT GAG TAC CTG GCC CCC GAG GTG        960
Thr Met Lys Thr Phe Cys Gly Thr Pro Glu Tyr Leu Ala Pro Glu Val
305             310             315             320

CTG GAG GAC AAT GAC TAC GGC CGT GCA GTG GAC TGG TGG GGG CTG GGC        1008
Leu Glu Asp Asn Asp Tyr Gly Arg Ala Val Asp Trp Trp Gly Leu Gly
                325             330             335

GTG GTC ATG TAC GAG ATG ATG TGC GGT CGC CTG CCC TTC TAC AAC CAG        1056
Val Val Met Tyr Glu Met Met Cys Gly Arg Leu Pro Phe Tyr Asn Gln
        340             345             350

GAC CAT GAG AAG CTT TTT GAG CTC ATC CTC ATG GAG GAG ATC CGC TTC        1104
Asp His Glu Lys Leu Phe Glu Leu Ile Leu Met Glu Glu Ile Arg Phe
        355             360             365

CCG CGC ACG CTT GGT CCC GAG GCC AAG TCC TTG CTT TCA GGG CTG CTC        1152
Pro Arg Thr Leu Gly Pro Glu Ala Lys Ser Leu Leu Ser Gly Leu Leu
        370             375             380

AAG AAG GAC CCC AAG CAG AGG CTT GGC GGG GGC TCC GAG GAC GCC AAG        1200
Lys Lys Asp Pro Lys Gln Arg Leu Gly Gly Gly Ser Glu Asp Ala Lys
385             390             395             400

GAG ATC ATG CAG CAT CGC TTC TTT GCC GGT ATC GTG TGG CAG CAC GTG        1248
Glu Ile Met Gln His Arg Phe Phe Ala Gly Ile Val Trp Gln His Val
                405             410             415

TAC GAG AAG AAG CTC AGC CCA CCC TTC AAG CCC CAG GTC ACG TCG GAG        1296
Tyr Glu Lys Lys Leu Ser Pro Pro Phe Lys Pro Gln Val Thr Ser Glu
        420             425             430

ACT GAC ACC AGG TAT TTT GAT GAG GAG TTC ACG GCC CAG ATG ATC ACC        1344
Thr Asp Thr Arg Tyr Phe Asp Glu Glu Phe Thr Ala Gln Met Ile Thr
        435             440             445

ATC ACA CCA CCT GAC CAA GAT GAC AGC ATG GAG TGT GTG GAC AGC GAG        1392
Ile Thr Pro Pro Asp Gln Asp Asp Ser Met Glu Cys Val Asp Ser Glu
        450             455             460

CGC AGG CCC CAC TTC CCC CAG TTC TCC TAC TCG GCC AGC AGC ACG GCC        1440
Arg Arg Pro His Phe Pro Gln Phe Ser Tyr Ser Ala Ser Ser Thr Ala
465             470             475             480

TCG GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC        1488
Ser Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe
                485             490             495
```

SUBSTITUTE SHEET (RULE 26)

```
     ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC    1536
     Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly
                 500             505             510
 5
     CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC    1584
     His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly
                 515             520             525
10   AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC    1632
     Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro
                 530             535             540
     TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC    1680
15   Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser
     545                 550             555             560
     CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG    1728
     Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met
                 565             570             575
20
     CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC    1776
     Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly
                 580             585             590
25
     AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG    1824
     Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val
                 595             600             605
30   AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC    1872
     Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile
                 610             615             620
     CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC    1920
35   Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile
     625                 630             635             640
     ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC    1968
     Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
                 645             650             655
40
     CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG    2016
     His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
                 660             665             670
45
     AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC    2064
     Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
                 675             680             685
50   CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT    2112
     Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
                 690             695             700
     CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC    2160
55   His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
     705                 710             715             720
```

```
ATG GAC GAG CTG TAC AAG TAA                                          2181
Met Asp Glu Leu Tyr Lys
                725
```

(2) INFORMATION FOR SEQ ID NO:71:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 726 amino acids
        (B) TYPE: amino acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: protein
    (v) FRAGMENT TYPE: internal

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

```
Met Ser Asp Val Ala Ile Val Lys Glu Gly Trp Leu His Lys Arg Gly
 1               5                  10                  15
Glu Tyr Ile Lys Thr Trp Arg Pro Arg Tyr Phe Leu Leu Lys Asn Asp
            20                  25                  30
Gly Thr Phe Ile Gly Tyr Lys Glu Arg Pro Gln Asp Val Asp Gln Arg
            35                  40                  45
Glu Ala Pro Leu Asn Asn Phe Ser Val Ala Gln Cys Gln Leu Met Lys
        50                  55                  60
Thr Glu Arg Pro Arg Pro Asn Thr Phe Ile Ile Arg Cys Leu Gln Trp
65                  70                  75                  80
Thr Thr Val Ile Glu Arg Thr Phe His Val Glu Thr Pro Glu Glu Arg
                85                  90                  95
Glu Glu Trp Thr Thr Ala Ile Gln Thr Val Ala Asp Gly Leu Lys Lys
                100                 105                 110
Gln Glu Glu Glu Glu Met Asp Phe Arg Ser Gly Ser Pro Ser Asp Asn
        115                 120                 125
Ser Gly Ala Glu Glu Met Glu Val Ser Leu Ala Lys Pro Lys His Arg
        130                 135                 140
Val Thr Met Asn Glu Phe Glu Tyr Leu Lys Leu Leu Gly Lys Gly Thr
145                 150                 155                 160
Phe Gly Lys Val Ile Leu Val Lys Glu Lys Ala Thr Gly Arg Tyr Tyr
                165                 170                 175
Ala Met Lys Ile Leu Lys Lys Glu Val Ile Val Ala Lys Asp Glu Val
                180                 185                 190
Ala His Thr Leu Thr Glu Asn Arg Val Leu Gln Asn Ser Arg His Pro
        195                 200                 205
Phe Leu Thr Ala Leu Lys Tyr Ser Phe Gln Thr His Asp Arg Leu Cys
        210                 215                 220
Phe Val Met Glu Tyr Ala Asn Gly Gly Glu Leu Phe Phe His Leu Ser
225                 230                 235                 240
Arg Glu Arg Val Phe Ser Glu Asp Arg Ala Arg Phe Tyr Gly Ala Glu
                245                 250                 255
Ile Val Ser Ala Leu Asp Tyr Leu His Ser Glu Lys Asn Val Val Tyr
                260                 265                 270
Arg Asp Leu Lys Leu Glu Asn Leu Met Leu Asp Lys Asp Gly His Ile
        275                 280                 285
Lys Ile Thr Asp Phe Gly Leu Cys Lys Glu Gly Ile Lys Asp Gly Ala
```

```
                290                           295                           300
        Thr Met Lys Thr Phe Cys Gly Thr Pro Glu Tyr Leu Ala Pro Glu Val
        305                           310                           315                           320
5       Leu Glu Asp Asn Asp Tyr Gly Arg Ala Val Asp Trp Trp Gly Leu Gly
                            325                           330                           335
        Val Val Met Tyr Glu Met Met Cys Gly Arg Leu Pro Phe Tyr Asn Gln
                    340                           345                           350
        Asp His Glu Lys Leu Phe Glu Leu Ile Leu Met Glu Glu Ile Arg Phe
                    355                           360                           365
10      Pro Arg Thr Leu Gly Pro Glu Ala Lys Ser Leu Leu Ser Gly Leu Leu
                    370                           375                           380
        Lys Lys Asp Pro Lys Gln Arg Leu Gly Gly Gly Ser Glu Asp Ala Lys
        385                           390                           395                           400
        Glu Ile Met Gln His Arg Phe Phe Ala Gly Ile Val Trp Gln His Val
15                          405                           410                           415
        Tyr Glu Lys Lys Leu Ser Pro Pro Phe Lys Pro Gln Val Thr Ser Glu
                    420                           425                           430
        Thr Asp Thr Arg Tyr Phe Asp Glu Glu Phe Thr Ala Gln Met Ile Thr
                    435                           440                           445
20      Ile Thr Pro Pro Asp Gln Asp Asp Ser Met Glu Cys Val Asp Ser Glu
                    450                           455                           460
        Arg Arg Pro His Phe Pro Gln Phe Ser Tyr Ser Ala Ser Ser Thr Ala
        465                           470                           475                           480
        Ser Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe
25                          485                           490                           495
        Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly
                    500                           505                           510
        His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly
                    515                           520                           525
30      Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro
                    530                           535                           540
        Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser
        545                           550                           555                           560
        Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met
35                          565                           570                           575
        Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly
                    580                           585                           590
        Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val
                    595                           600                           605
40      Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile
                    610                           615                           620
        Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile
        625                           630                           635                           640
        Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
45                          645                           650                           655
        His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
                    660                           665                           670
        Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
                    675                           680                           685
50      Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
                    690                           695                           700
        His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
        705                           710                           715                           720
        Met Asp Glu Leu Tyr Lys
55                          725
```

(2) INFORMATION FOR SEQ ID NO:72:

    (i) SEQUENCE CHARACTERISTICS:
      (A) LENGTH: 2751 base pairs
5   (B) TYPE: nucleic acid
      (C) STRANDEDNESS: single
      (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA
10   (ix) FEATURE:

      (A) NAME/KEY: Coding Sequence
      (B) LOCATION: 1...2748
      (D) OTHER INFORMATION:
15

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

```
     ATG GCT GAC GTT TAC CCG GCC AAC GAC TCC ACG GCG TCT CAG GAC GTG        48
     Met Ala Asp Val Tyr Pro Ala Asn Asp Ser Thr Ala Ser Gln Asp Val
20   1               5                   10                  15

     GCC AAC CGC TTC GCC CGC AAA GGG GCG CTG AGG CAG AAG AAC GTG CAT        96
     Ala Asn Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His
                 20                  25                  30
25

     GAG GTG AAA GAC CAC AAA TTC ATC GCC CGC TTC TTC AAG CAA CCC ACC       144
     Glu Val Lys Asp His Lys Phe Ile Ala Arg Phe Phe Lys Gln Pro Thr
                 35                  40                  45

30   TTC TGC AGC CAC TGC ACC GAC TTC ATC TGG GGG TTT GGG AAA CAA GGC       192
     Phe Cys Ser His Cys Thr Asp Phe Ile Trp Gly Phe Gly Lys Gln Gly
                 50                  55                  60

     TTC CAG TGC CAA GTT TGC TGT TTT GTG GTT CAT AAG AGG TGC CAT GAG       240
35   Phe Gln Cys Gln Val Cys Cys Phe Val Val His Lys Arg Cys His Glu
     65                  70                  75                  80

     TTC GTT ACG TTC TCT TGT CCG GGT GCG GAT AAG GGA CCT GAC ACT GAC       288
     Phe Val Thr Phe Ser Cys Pro Gly Ala Asp Lys Gly Pro Asp Thr Asp
40                       85                  90                  95

     GAC CCC AGG AGC AAG CAC AAG TTC AAA ATC CAC ACA TAC GGA AGC CCT       336
     Asp Pro Arg Ser Lys His Lys Phe Lys Ile His Thr Tyr Gly Ser Pro
                 100                 105                 110
45

     ACC TTC TGT GAT CAC TGT GGG TCC CTG CTC TAT GGA CTT ATC CAC CAA       384
     Thr Phe Cys Asp His Cys Gly Ser Leu Leu Tyr Gly Leu Ile His Gln
                 115                 120                 125

50   GGG ATG AAA TGT GAC ACC TGC GAC ATG AAT GTT CAC AAC CAG TGT GTG       432
     Gly Met Lys Cys Asp Thr Cys Asp Met Asn Val His Asn Gln Cys Val
                 130                 135                 140

     ATC AAT GAC CCT AGC CTC TGC GGA ATG GAT CAC ACA GAG AAG AGG GGG       480
55   Ile Asn Asp Pro Ser Leu Cys Gly Met Asp His Thr Glu Lys Arg Gly
     145                 150                 155                 160
```

160

```
    CGG ATT TAT CTG AAG GCT GAG GTC ACT GAT GAA AAG CTC CAC GTC ACG    528
    Arg Ile Tyr Leu Lys Ala Glu Val Thr Asp Glu Lys Leu His Val Thr
                    165                 170                 175
 5
    GTA CGA GAT GCA AAA AAT CTA ATC CCT ATG GAT CCA AAT GGG CTT TCG    576
    Val Arg Asp Ala Lys Asn Leu Ile Pro Met Asp Pro Asn Gly Leu Ser
                    180                 185                 190

10  GAT CCT TAT GTG AAG CTG AAA CTA ATC CCT GAC CCC AAG AAT GAG AGC    624
    Asp Pro Tyr Val Lys Leu Lys Leu Ile Pro Asp Pro Lys Asn Glu Ser
                    195                 200                 205

    AAA CAG AAA ACC AAA ACC ATC CGC TCC AAC CTG AAT CCT CAG TGG AAT    672
15  Lys Gln Lys Thr Lys Thr Ile Arg Ser Asn Leu Asn Pro Gln Trp Asn
                    210                 215                 220

    GAG TCC TTC ACG TTC AAA TTA AAA CCT TCA GAC AAA GAC CGG CGA CTG    720
    Glu Ser Phe Thr Phe Lys Leu Lys Pro Ser Asp Lys Asp Arg Arg Leu
20  225                 230                 235                 240

    TCT GTA GAA ATC TGG GAC TGG GAT CGG ACG ACT CGG AAT GAC TTC ATG    768
    Ser Val Glu Ile Trp Asp Trp Asp Arg Thr Thr Arg Asn Asp Phe Met
                    245                 250                 255
25
    GGA TCC CTT TCC TTT GGT GTC TCA GAG CTA ATG AAG ATG CCG GCC AGT    816
    Gly Ser Leu Ser Phe Gly Val Ser Glu Leu Met Lys Met Pro Ala Ser
                    260                 265                 270

30  GGA TGG TAT AAA GCT CAC AAC CAA GAA GAG GGC GAA TAT TAC AAC GTG    864
    Gly Trp Tyr Lys Ala His Asn Gln Glu Glu Gly Glu Tyr Tyr Asn Val
                    275                 280                 285

    CCC ATT CCA GAA GGA GAT GAA GAA GGC AAC ATG GAA CTC AGG CAG AAG    912
35  Pro Ile Pro Glu Gly Asp Glu Glu Gly Asn Met Glu Leu Arg Gln Lys
                    290                 295                 300

    TTT GAG AAA GCC AAG CTA GGT CCT GTT GGT AAC AAA GTC ATC AGC CCT    960
    Phe Glu Lys Ala Lys Leu Gly Pro Val Gly Asn Lys Val Ile Ser Pro
40  305                 310                 315                 320

    TCA GAA GAC AGA AAG CAA CCA TCC AAC AAC CTG GAC AGA GTG AAA CTC   1008
    Ser Glu Asp Arg Lys Gln Pro Ser Asn Asn Leu Asp Arg Val Lys Leu
                    325                 330                 335
45
    ACA GAC TTC AAC TTC CTC ATG GTG CTG GGG AAG GGG AGT TTT GGG AAG   1056
    Thr Asp Phe Asn Phe Leu Met Val Leu Gly Lys Gly Ser Phe Gly Lys
                    340                 345                 350

50  GTG ATG CTT GCT GAC AGG AAG GGA ACG GAG GAA CTG TAC GCC ATC AAG   1104
    Val Met Leu Ala Asp Arg Lys Gly Thr Glu Glu Leu Tyr Ala Ile Lys
                    355                 360                 365

    ATC CTG AAG AAG GAC GTG GTG ATC CAG GAC GAC GAC GTG GAG TGC ACC   1152
55  Ile Leu Lys Lys Asp Val Val Ile Gln Asp Asp Asp Val Glu Cys Thr
                    370                 375                 380
```

BNSDOCID: <WO___9845704A2_I_>

162

```
     ATG GTG GAG AAG CGC GTG CTG GCC CTG CTG GAC AAG CCG CCA TTT CTG    1200
     Met Val Glu Lys Arg Val Leu Ala Leu Leu Asp Lys Pro Pro Phe Leu
     385             390             395             400
  5

     ACA CAG CTG CAC TCC TGC TTC CAG ACA GTG GAC CGG CTG TAC TTC GTC    1248
     Thr Gln Leu His Ser Cys Phe Gln Thr Val Asp Arg Leu Tyr Phe Val
                     405             410             415

 10  ATG GAA TAC GTC AAC GGC GGG GAT CTT ATG TAC CAC ATT CAG CAA GTC    1296
     Met Glu Tyr Val Asn Gly Gly Asp Leu Met Tyr His Ile Gln Gln Val
                 420             425             430

     GGG AAA TTT AAG GAG CCA CAA GCA GTA TTC TAC GCA GCC GAG ATC TCC    1344
 15  Gly Lys Phe Lys Glu Pro Gln Ala Val Phe Tyr Ala Ala Glu Ile Ser
                 435             440             445

     ATC GGA CTG TTC TTC CTT CAT AAA AGA GGG ATC ATT TAC AGG GAT CTG    1392
     Ile Gly Leu Phe Phe Leu His Lys Arg Gly Ile Ile Tyr Arg Asp Leu
 20  450             455             460

     AAG CTG AAC AAT GTC ATG CTG AAC TCA GAA GGG CAC ATC AAA ATC GCC    1440
     Lys Leu Asn Asn Val Met Leu Asn Ser Glu Gly His Ile Lys Ile Ala
     465             470             475             480
 25

     GAC TTC GGG ATG TGC AAG GAA CAC ATG ATG GAT GGA GTC ACG ACC AGG    1488
     Asp Phe Gly Met Cys Lys Glu His Met Met Asp Gly Val Thr Thr Arg
                     485             490             495

 30  ACC TTC TGC GGA ACT CCG GAC TAC ATT GCC CCA GAG ATA ATC GCT TAC    1536
     Thr Phe Cys Gly Thr Pro Asp Tyr Ile Ala Pro Glu Ile Ile Ala Tyr
                 500             505             510

     CAG CCG TAC GGG AAG TCT GTA GAT TGG TGG GCG TAC GGT GTG CTG CTG    1584
 35  Gln Pro Tyr Gly Lys Ser Val Asp Trp Trp Ala Tyr Gly Val Leu Leu
                 515             520             525

     TAC GAG ATG CTA GCC GGG CAG CCT CCG TTT GAT GGT GAA GAT GAA GAT    1632
     Tyr Glu Met Leu Ala Gly Gln Pro Pro Phe Asp Gly Glu Asp Glu Asp
 40      530             535             540

     GAA CTG TTT CAG TCT ATA ATG GAG CAC AAC GTG TCC TAC CCC AAA TCC    1680
     Glu Leu Phe Gln Ser Ile Met Glu His Asn Val Ser Tyr Pro Lys Ser
     545             550             555             560
 45

     TTG TCC AAG GAA GCC GTC TCC ATC TGC AAA GGA CTT ATG ACC AAA CAG    1728
     Leu Ser Lys Glu Ala Val Ser Ile Cys Lys Gly Leu Met Thr Lys Gln
                     565             570             575

 50  CCT GCC AAG CGA CTG GGC TGC GGG CCC GAG GGA GAG AGG GAT GTC AGA    1776
     Pro Ala Lys Arg Leu Gly Cys Gly Pro Glu Gly Glu Arg Asp Val Arg
                     580             585             590

     GAG CAT GCC TTC TTC AGG AGG ATC GAC TGG GAG AAA CTG GAG AAC AGG    1824
 55  Glu His Ala Phe Phe Arg Arg Ile Asp Trp Glu Lys Leu Glu Asn Arg
                 595             600             605
```

162

BNSDOCID: <WO___9845704A2_I_>

```
        GAG ATC CAA CCA CCA TTC AAG CCC AAA GTG TGT GGC AAA GGA GCA GAA      1872
        Glu Ile Gln Pro Pro Phe Lys Pro Lys Val Cys Gly Lys Gly Ala Glu
            610             615             620
  5
        AAC TTT GAC AAG TTC TTC ACG CGA GGA CAG CCT GTC TTA ACA CCA CCA      1920
        Asn Phe Asp Lys Phe Phe Thr Arg Gly Gln Pro Val Leu Thr Pro Pro
        625             630             635             640

 10     GAT CAG CTG GTC ATT GCT AAC ATA GAC CAA TCT GAT TTT GAA GGG TTC      1968
        Asp Gln Leu Val Ile Ala Asn Ile Asp Gln Ser Asp Phe Glu Gly Phe
                        645             650             655

        TCG TAT GTC AAC CCC CAG TTT GTG CAC CCA ATC TTG CAA AGT GCA GTA      2016
 15     Ser Tyr Val Asn Pro Gln Phe Val His Pro Ile Leu Gln Ser Ala Val
                        660             665             670

        GGG CGC GCC ATG AGT AAA GGA GAA GAA CTT TTC ACT GGA GTT GTC CCA      2064
        Gly Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
 20                     675             680             685

        ATT CTT GTT GAA TTA GAT GGC GAT GTT AAT GGG CAA AAA TTC TCT GTT      2112
        Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val
            690             695             700
 25
        AGT GGA GAG GGT GAA GGT GAT GCA ACA TAC GGA AAA CTT ACC CTT AAA      2160
        Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
        705             710             715             720

 30     TTT ATT TGC ACT ACT GGG AAG CTA CCT GTT CCA TGG CCA ACG CTT GTC      2208
        Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
                        725             730             735

        ACT ACT CTC ACT TAT GGT GTT CAA TGC TTT TCT AGA TAC CCA GAT CAT      2256
 35     Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
                        740             745             750

        ATG AAA CAG CAT GAC TTT TTC AAG AGT GCC ATG CCC GAA GGT TAT GTA      2304
        Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
 40                 755             760             765

        CAG GAA AGA ACT ATA TTT TAC AAA GAT GAC GGG AAC TAC AAG ACA CGT      2352
        Gln Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg
                770             775             780
 45
        GCT GAA GTC AAG TTT GAA GGT GAT ACC CTT GTT AAT AGA ATC GAG TTA      2400
        Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
        785             790             795             800

 50     AAA GGT ATT GAT TTT AAA GAA GAT GGA AAC ATT CTT GGA CAC AAA ATG      2448
        Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met
                        805             810             815

        GAA TAC AAT TAT AAC TCA CAT AAT GTA TAC ATC ATG GCA GAC AAA CCA      2496
 55     Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro
                        820             825             830
```

163

SUBSTITUTE SHEET (RULE 26)

164

```
    AAG AAT GGC ATC AAA GTT AAC TTC AAA ATT AGA CAC AAC ATT AAA GAT    2544
    Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp
            835             840             845
5

    GGA AGC GTT CAA TTA GCA GAC CAT TAT CAA CAA AAT ACT CCA ATT GGC    2592
    Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
            850             855             860

10  GAT GGC CCT GTC CTT TTA CCA GAC AAC CAT TAC CTG TCC ACG CAA TCT    2640
    Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
    865             870             875             880

    GCC CTT TCC AAA GAT CCC AAC GAA AAG AGA GAT CAC ATG ATC CTT CTT    2688
15  Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu
                    885             890             895

    GAG TTT GTA ACA GCT GCT GGG ATT ACA CAT GGC ATG GAT GAA CTA TAC    2736
    Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr
20                  900             905             910

    AAA CCT CAG GAG TAA                                                2751
    Lys Pro Gln Glu
            915
25


        (2) INFORMATION FOR SEQ ID NO:73:

        (i) SEQUENCE CHARACTERISTICS:
30          (A) LENGTH: 916 amino acids
            (B) TYPE: amino acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

35      (ii) MOLECULE TYPE: protein
        (v) FRAGMENT TYPE: internal

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

40  Met Ala Asp Val Tyr Pro Ala Asn Asp Ser Thr Ala Ser Gln Asp Val
    1               5               10              15
    Ala Asn Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His
                20              25              30
    Glu Val Lys Asp His Lys Phe Ile Ala Arg Phe Phe Lys Gln Pro Thr
45          35              40              45
    Phe Cys Ser His Cys Thr Asp Phe Ile Trp Gly Phe Gly Lys Gln Gly
            50              55              60
    Phe Gln Cys Gln Val Cys Cys Phe Val Val His Lys Arg Cys His Glu
    65              70              75              80
50  Phe Val Thr Phe Ser Cys Pro Gly Ala Asp Lys Gly Pro Asp Thr Asp
                    85              90              95
    Asp Pro Arg Ser Lys His Lys Phe Lys Ile His Thr Tyr Gly Ser Pro
                100             105             110
    Thr Phe Cys Asp His Cys Gly Ser Leu Leu Tyr Gly Leu Ile His Gln
55          115             120             125
    Gly Met Lys Cys Asp Thr Cys Asp Met Asn Val His Asn Gln Cys Val
```

BNSDOCID: <WO___9845704A2_I_>

```
              130                 135                 140
     Ile Asn Asp Pro Ser Leu Cys Gly Met Asp His Thr Glu Lys Arg Gly
     145                 150                 155                 160
     Arg Ile Tyr Leu Lys Ala Glu Val Thr Asp Glu Lys Leu His Val Thr
  5                      165                 170                 175
     Val Arg Asp Ala Lys Asn Leu Ile Pro Met Asp Pro Asn Gly Leu Ser
                     180                 185                 190
     Asp Pro Tyr Val Lys Leu Lys Leu Ile Pro Asp Pro Lys Asn Glu Ser
                     195                 200                 205
 10  Lys Gln Lys Thr Lys Thr Ile Arg Ser Asn Leu Asn Pro Gln Trp Asn
                 210                 215                 220
     Glu Ser Phe Thr Phe Lys Leu Lys Pro Ser Asp Lys Asp Arg Arg Leu
     225                 230                 235                 240
     Ser Val Glu Ile Trp Asp Trp Asp Arg Thr Thr Arg Asn Asp Phe Met
 15                  245                 250                 255
     Gly Ser Leu Ser Phe Gly Val Ser Glu Leu Met Lys Met Pro Ala Ser
                     260                 265                 270
     Gly Trp Tyr Lys Ala His Asn Gln Glu Glu Gly Glu Tyr Tyr Asn Val
                 275                 280                 285
 20  Pro Ile Pro Glu Gly Asp Glu Glu Gly Asn Met Glu Leu Arg Gln Lys
             290                 295                 300
     Phe Glu Lys Ala Lys Leu Gly Pro Val Gly Asn Lys Val Ile Ser Pro
     305                 310                 315                 320
     Ser Glu Asp Arg Lys Gln Pro Ser Asn Asn Leu Asp Arg Val Lys Leu
 25                  325                 330                 335
     Thr Asp Phe Asn Phe Leu Met Val Leu Gly Lys Gly Ser Phe Gly Lys
                 340                 345                 350
     Val Met Leu Ala Asp Arg Lys Gly Thr Glu Glu Leu Tyr Ala Ile Lys
             355                 360                 365
 30  Ile Leu Lys Lys Asp Val Val Ile Gln Asp Asp Asp Val Glu Cys Thr
         370                 375                 380
     Met Val Glu Lys Arg Val Leu Ala Leu Leu Asp Lys Pro Pro Phe Leu
     385                 390                 395                 400
     Thr Gln Leu His Ser Cys Phe Gln Thr Val Asp Arg Leu Tyr Phe Val
 35                  405                 410                 415
     Met Glu Tyr Val Asn Gly Gly Asp Leu Met Tyr His Ile Gln Gln Val
                 420                 425                 430
     Gly Lys Phe Lys Glu Pro Gln Ala Val Phe Tyr Ala Ala Glu Ile Ser
             435                 440                 445
 40  Ile Gly Leu Phe Phe Leu His Lys Arg Gly Ile Ile Tyr Arg Asp Leu
         450                 455                 460
     Lys Leu Asn Asn Val Met Leu Asn Ser Glu Gly His Ile Lys Ile Ala
     465                 470                 475                 480
     Asp Phe Gly Met Cys Lys Glu His Met Met Asp Gly Val Thr Thr Arg
 45                  485                 490                 495
     Thr Phe Cys Gly Thr Pro Asp Tyr Ile Ala Pro Glu Ile Ile Ala Tyr
             500                 505                 510
     Gln Pro Tyr Gly Lys Ser Val Asp Trp Trp Ala Tyr Gly Val Leu Leu
         515                 520                 525
 50  Tyr Glu Met Leu Ala Gly Gln Pro Pro Phe Asp Gly Glu Asp Glu Asp
         530                 535                 540
     Glu Leu Phe Gln Ser Ile Met Glu His Asn Val Ser Tyr Pro Lys Ser
     545                 550                 555                 560
     Leu Ser Lys Glu Ala Val Ser Ile Cys Lys Gly Leu Met Thr Lys Gln
 55                  565                 570                 575
     Pro Ala Lys Arg Leu Gly Cys Gly Pro Glu Gly Glu Arg Asp Val Arg
```

SUBSTITUTE SHEET (RULE 26)

```
                    580                    585                    590
      Glu His Ala Phe Phe Arg Arg Ile Asp Trp Glu Lys Leu Glu Asn Arg
              595                    600                    605
 5    Glu Ile Gln Pro Pro Phe Lys Pro Lys Val Cys Gly Lys Gly Ala Glu
              610                    615                    620
      Asn Phe Asp Lys Phe Phe Thr Arg Gly Gln Pro Val Leu Thr Pro Pro
      625                    630                    635                    640
      Asp Gln Leu Val Ile Ala Asn Ile Asp Gln Ser Asp Phe Glu Gly Phe
                          645                    650                    655
10    Ser Tyr Val Asn Pro Gln Phe Val His Pro Ile Leu Gln Ser Ala Val
                  660                    665                    670
      Gly Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
              675                    680                    685
      Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val
15            690                    695                    700
      Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
      705                    710                    715                    720
      Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
                          725                    730                    735
20    Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
                  740                    745                    750
      Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
              755                    760                    765
      Gln Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg
25            770                    775                    780
      Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
      785                    790                    795                    800
      Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met
                          805                    810                    815
30    Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro
                  820                    825                    830
      Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp
              835                    840                    845
      Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
35            850                    855                    860
      Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
      865                    870                    875                    880
      Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu
                          885                    890                    895
40    Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr
                  900                    905                    910
      Lys Pro Gln Glu
              915
```

45   (2) INFORMATION FOR SEQ ID NO:74:

            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 2157 base pairs
                (B) TYPE: nucleic acid
50   (C) STRANDEDNESS: single
                (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: cDNA
            (ix) FEATURE:
55
                (A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...2154
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

```
5
      ATG TCG TCC ATC TTG CCA TTC ACG CCG CCA GTT GTG AAG AGA CTG CTG    48
      Met Ser Ser Ile Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu
      1               5                   10                  15

10    GGA TGG AAG AAG TCA GCT GGT GGG TCT GGA GGA GCA GGC GGA GGA GAG    96
      Gly Trp Lys Lys Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu
                  20                  25                  30

      CAG AAT GGG CAG GAA GAA AAG TGG TGT GAG AAA GCA GTG AAA AGT CTG    144
15    Gln Asn Gly Gln Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu
                      35                  40                  45

      GTG AAG AAG CTA AAG AAA ACA GGA CGA TTA GAT GAG CTT GAG AAA GCC    192
      Val Lys Lys Leu Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala
20        50                  55                  60

      ATC ACC ACT CAA AAC TGT AAT ACT AAA TGT GTT ACC ATA CCA AGC ACT    240
      Ile Thr Thr Gln Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr
      65                  70                  75                  80
25
      TGC TCT GAA ATT TGG GGA CTG AGT ACA CCA AAT ACG ATA GAT CAG TGG    288
      Cys Ser Glu Ile Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp
                          85                  90                  95

30    GAT ACA ACA GGC CTT TAC AGC TTC TCT GAA CAA ACC AGG TCT CTT GAT    336
      Asp Thr Thr Gly Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp
                          100                 105                 110

      GGT CGT CTC CAG GTA TCC CAT CGA AAA GGA TTG CCA CAT GTT ATA TAT    384
35    Gly Arg Leu Gln Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr
                      115                 120                 125

      TGC CGA TTA TGG CGC TGG CCT GAT CTT CAC AGT CAT CAT GAA CTC AAG    432
      Cys Arg Leu Trp Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys
40        130                 135                 140

      GCA ATT GAA AAC TGC GAA TAT GCT TTT AAT CTT AAA AAG GAT GAA GTA    480
      Ala Ile Glu Asn Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val
      145                 150                 155                 160
45
      TGT GTA AAC CCT TAC CAC TAT CAG AGA GTT GAG ACA CCA GTT TTG CCT    528
      Cys Val Asn Pro Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro
                          165                 170                 175

50    CCA GTA TTA GTG CCC CGA CAC ACC GAG ATC CTA ACA GAA CTT CCG CCT    576
      Pro Val Leu Val Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro
                      180                 185                 190

      CTG GAT GAC TAT ACT CAC TCC ATT CCA GAA AAC ACT AAC TTC CCA GCA    624
55    Leu Asp Asp Tyr Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala
                  195                 200                 205
```

```
      GGA ATT GAG CCA CAG AGT AAT TAT ATT CCA GAA ACG CCA CCT CCT GGA    672
      Gly Ile Glu Pro Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly
          210             215             220
 5
      TAT ATC AGT GAA GAT GGA GAA ACA AGT GAC CAA CAG TTG AAT CAA AGT    720
      Tyr Ile Ser Glu Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser
      225             230             235             240

10    ATG GAC ACA GGC TCT CCA GCA GAA CTA TCT CCT ACT ACT CTT TCC CCT    768
      Met Asp Thr Gly Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro
                  245             250             255

      GTT AAT CAT AGC TTG GAT TTA CAG CCA GTT ACT TAC TCA GAA CCT GCA    816
 15   Val Asn His Ser Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala
                  260             265             270

      TTT TGG TGT TCA ATA GCA TAT TAT GAA TTA AAT CAG AGG GTT GGA GAA    864
      Phe Trp Cys Ser Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu
 20       275             280             285

      ACC TTC CAT GCA TCA CAG CCC TCA CTC ACT GTA GAT GGC TTT ACA GAC    912
      Thr Phe His Ala Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp
          290             295             300
 25
      CCA TCA AAT TCA GAG AGG TTC TGC TTA GGT TTA CTC TCC AAT GTT AAC    960
      Pro Ser Asn Ser Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn
      305             310             315             320

 30   CGA AAT GCC ACG GTA GAA ATG ACA AGA AGG CAT ATA GGA AGA GGA GTG   1008
      Arg Asn Ala Thr Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val
                  325             330             335

      CGC TTA TAC TAC ATA GGT GGG GAA GTT TTT GCT GAG TGC CTA AGT GAT   1056
 35   Arg Leu Tyr Tyr Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp
                  340             345             350

      AGT GCA ATC TTT GTG CAG AGC CCC AAT TGT AAT CAG AGA TAT GGC TGG   1104
      Ser Ala Ile Phe Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp
 40       355             360             365

      CAC CCT GCA ACA GTG TGT AAA ATT CCA CCA GGC TGT AAT CTG AAG ATC   1152
      His Pro Ala Thr Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile
          370             375             380
 45
      TTC AAC AAC CAG GAA TTT GCT GCT CTT CTG GCT CAG TCT GTT AAT CAG   1200
      Phe Asn Asn Gln Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln
      385             390             395             400

 50   GGT TTT GAA GCC GTC TAT CAG CTA ACT AGA ATG TGC ACC ATA AGA ATG   1248
      Gly Phe Glu Ala Val Tyr Gln Leu Thr Arg Met Cys Thr Ile Arg Met
                  405             410             415

      AGT TTT GTG AAA GGG TGG GGA GCA GAA TAC CGA AGG CAG ACG GTA ACA   1296
 55   Ser Phe Val Lys Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr
                  420             425             430
```

SUBSTITUTE SHEET (RULE 26)

```
     AGT ACT CCT TGC TGG ATT GAA CTT CAT CTG AAT GGA CCT CTA CAG TGG   1344
     Ser Thr Pro Cys Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp
             435                 440                 445
 5
     TTG GAC AAA GTA TTA ACT CAG ATG GGA TCC CCT TCA GTG CGT TGC TCA   1392
     Leu Asp Lys Val Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser
             450                 455                 460

10   AGC ATG TCA TGG GTA CCG CGG GCC CGG GAT CCA CCG GTC GCC ACC ATG   1440
     Ser Met Ser Trp Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met
     465                 470                 475                 480

     GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC   1488
15   Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                         485                 490                 495

     GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG   1536
     Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
20                       500                 505                 510

     GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC   1584
     Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
                 515                 520                 525
25
     ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG   1632
     Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
             530                 535                 540

30   ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG   1680
     Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
     545                 550                 555                 560

     CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC   1728
35   His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                         565                 570                 575

     ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG   1776
     Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
40                       580                 585                 590

     AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC   1824
     Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
                 595                 600                 605
45
     GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC   1872
     Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
             610                 615                 620

50   TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC   1920
     Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
     625                 630                 635                 640

     ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG   1968
55   Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
                         645                 650                 655
```

SUBSTITUTE SHEET (RULE 26)

170

```
    CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC      2016
    Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
                    660                 665             670
 5
    GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC      2064
    Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
                    675             680                 685

10  AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG      2112
    Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
                690             695             700

    ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA         2157
15  Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
    705             710             715


          (2)  INFORMATION FOR SEQ ID NO:75:
20
          (i)  SEQUENCE CHARACTERISTICS:
               (A)  LENGTH: 718 amino acids
               (B)  TYPE: amino acid
               (C)  STRANDEDNESS: single
25             (D)  TOPOLOGY: linear

          (ii)  MOLECULE TYPE: protein
          (v)  FRAGMENT TYPE: internal

30        (xi)  SEQUENCE DESCRIPTION: SEQ ID NO:75:

    Met Ser Ser Ile Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu
    1             5               10              15
    Gly Trp Lys Lys Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu
35            20              25              30
    Gln Asn Gly Gln Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu
            35              40              45
    Val Lys Lys Leu Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala
            50              55              60
40  Ile Thr Thr Gln Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr
    65              70              75              80
    Cys Ser Glu Ile Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp
                    85              90              95
    Asp Thr Thr Gly Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp
45                  100             105             110
    Gly Arg Leu Gln Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr
            115             120             125
    Cys Arg Leu Trp Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys
            130             135             140
50  Ala Ile Glu Asn Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val
    145             150             155             160
    Cys Val Asn Pro Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro
                    165             170             175
    Pro Val Leu Val Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro
55                  180             185             190
    Leu Asp Asp Tyr Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala
```

```
                195                   200                   205
        Gly Ile Glu Pro Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly
            210                   215                   220
        Tyr Ile Ser Glu Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser
 5      225                   230                   235                   240
        Met Asp Thr Gly Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro
                            245                   250                   255
        Val Asn His Ser Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala
                260                   265                   270
10      Phe Trp Cys Ser Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu
            275                   280                   285
        Thr Phe His Ala Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp
            290                   295                   300
        Pro Ser Asn Ser Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn
15      305                   310                   315                   320
        Arg Asn Ala Thr Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val
                            325                   330                   335
        Arg Leu Tyr Tyr Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp
                340                   345                   350
20      Ser Ala Ile Phe Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp
            355                   360                   365
        His Pro Ala Thr Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile
            370                   375                   380
        Phe Asn Asn Gln Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln
25      385                   390                   395                   400
        Gly Phe Glu Ala Val Tyr Gln Leu Thr Arg Met Cys Thr Ile Arg Met
                            405                   410                   415
        Ser Phe Val Lys Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr
                420                   425                   430
30      Ser Thr Pro Cys Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp
            435                   440                   445
        Leu Asp Lys Val Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser
            450                   455                   460
        Ser Met Ser Trp Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met
35      465                   470                   475                   480
        Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                            485                   490                   495
        Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
                500                   505                   510
40      Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
            515                   520                   525
        Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
            530                   535                   540
        Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
45      545                   550                   555                   560
        His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                            565                   570                   575
        Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
                580                   585                   590
50      Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
            595                   600                   605
        Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
            610                   615                   620
        Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
55      625                   630                   635                   640
        Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
```

172

```
                        645                  650                    655
        Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
                    660                  665                    670
        Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
   5                675                  680                    685
        Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
                    690                  695                    700
        Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
        705                  710                  715
  10

            (2) INFORMATION FOR SEQ ID NO:76:

            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 2397 base pairs
  15            (B) TYPE: nucleic acid
                (C) STRANDEDNESS: single
                (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: cDNA
  20        (ix) FEATURE:

                (A) NAME/KEY: Coding Sequence
                (B) LOCATION: 1...2394
                (D) OTHER INFORMATION:
  25
            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

        ATG GAC AAT ATG TCT ATT ACG AAT ACA CCA ACA AGT AAT GAT GCC TGT       48
        Met Asp Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys
  30    1               5                   10                  15

        CTG AGC ATT GTG CAT AGT TTG ATG TGC CAT AGA CAA GGT GGA GAG AGT       96
        Leu Ser Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser
                    20                  25                  30
  35
        GAA ACA TTT GCA AAA AGA GCA ATT GAA AGT TTG GTA AAG AAG CTG AAG      144
        Glu Thr Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys
                    35                  40                  45

  40    GAG AAA AAA GAT GAA TTG GAT TCT TTA ATA ACA GCT ATA ACT ACA AAT      192
        Glu Lys Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn
                    50                  55                  60

        GGA GCT CAT CCT AGT AAA TGT GTT ACC ATA CAG AGA ACA TTG GAT GGG      240
  45    Gly Ala His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly
        65                  70                  75                  80

        AGG CTT CAG GTG GCT GGT CGG AAA GGA TTT CCT CAT GTG ATC TAT GCC      288
        Arg Leu Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala
  50                        85                  90                  95

        CGT CTC TGG AGG TGG CCT GAT CTT CAC AAA AAT GAA CTA AAA CAT GTT      336
        Arg Leu Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val
                        100                 105                 110
  55
        AAA TAT TGT CAG TAT GCG TTT GAC TTA AAA TGT GAT AGT GTC TGT GTG      384
```

173

```
          Lys Tyr Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val
              115                     120                 125

    AAT CCA TAT CAC TAC GAA CGA GTT GTA TCA CCT GGA ATT GAT CTC TCA    432
5   Asn Pro Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser
        130                     135                 140

    GGA TTA ACA CTG CAG AGT AAT GCT CCA TCA AGT ATG ATG GTG AAG GAT    480
    Gly Leu Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp
10  145                 150                 155                 160

    GAA TAT GTG CAT GAC TTT GAG GGA CAG CCA TCG TTG TCC ACT GAA GGA    528
    Glu Tyr Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly
                        165                 170                 175
15
    CAT TCA ATT CAA ACC ATC CAG CAT CCA CCA AGT AAT CGT GCA TCG ACA    576
    His Ser Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr
                            180                 185                 190

20  GAG ACA TAC AGC ACC CCA GCT CTG TTA GCC CCA TCT GAG TCT AAT GCT    624
    Glu Thr Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala
                195                 200                 205

    ACC AGC ACT GCC AAC TTT CCC AAC ATT CCT GTG GCT TCC ACA AGT CAG    672
25  Thr Ser Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln
            210                 215                 220

    CCT GCC AGT ATA CTG GGG GGC AGC CAT AGT GAA GGA CTG TTG CAG ATA    720
    Pro Ala Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile
30  225                 230                 235                 240

    GCA TCA GGG CCT CAG CCA GGA CAG CAG CAG AAT GGA TTT ACT GGT CAG    768
    Ala Ser Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Gly Gln
                        245                 250                 255
35
    CCA GCT ACT TAC CAT CAT AAC AGC ACT ACC ACC TGG ACT GGA AGT AGG    816
    Pro Ala Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg
                    260                 265                 270

40  ACT GCA CCA TAC ACA CCT AAT TTG CCT CAC CAC CAA AAC GGC CAT CTT    864
    Thr Ala Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu
                275                 280                 285

    CAG CAC CAC CCG CCT ATG CCG CCC CAT CCC GGA CAT TAC TGG CCT GTT    912
45  Gln His His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val
            290                 295                 300

    CAC AAT GAG CTT GCA TTC CAG CCT CCC ATT TCC AAT CAT CCT GCT CCT    960
    His Asn Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Pro Ala Pro
50  305                 310                 315                 320

    GAG TAT TGG TGT TCC ATT GCT TAC TTT GAA ATG GAT GTT CAG GTA GGA   1008
    Glu Tyr Trp Cys Ser Ile Ala Tyr Phe Glu Met Asp Val Gln Val Gly
                        325                 330                 335
55
    GAG ACA TTT AAG GTT CCT TCA AGC TGC CCT ATT GTT ACT GTT GAT GGA   1056
```

173

174

```
           Glu Thr Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly
                       340                 345             350

  5        TAC GTG GAC CCT TCT GGA GGA GAT CGC TTT TGT TTG GGT CAA CTC TCC    1104
           Tyr Val Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser
                       355                 360             365

           AAT GTC CAC AGG ACA GAA GCC ATT GAG AGA GCA AGG TTG CAC ATA GGC    1152
           Asn Val His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly
  10               370                 375             380

           AAA GGT GTG CAG TTG GAA TGT AAA GGT GAA GGT GAT GTT TGG GTC AGG    1200
           Lys Gly Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg
           385                 390             395                 400
  15
           TGC CTT AGT GAC CAC GCG GTC TTT GTA CAG AGT TAC TAC TTA GAC AGA    1248
           Cys Leu Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg
                           405                 410             415

  20       GAA GCT GGG CGT GCA CCT GGA GAT GCT GTT CAT AAG ATC TAC CCA AGT    1296
           Glu Ala Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser
                       420                 425             430

           GCA TAT ATA AAG GTC TTT GAT TTG CGT CAG TGT CAT CGA CAG ATG CAG    1344
  25       Ala Tyr Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln
                       435                 440             445

           CAG CAG GCG GCT ACT GCA CAA GCT GCA GCA GCT GCC CAG GCA GCA GCC    1392
           Gln Gln Ala Ala Thr Ala Gln Ala Ala Ala Ala Ala Gln Ala Ala Ala
  30               450                 455             460

           GTG GCA GGA AAC ATC CCT GGC CCA GGA TCA GTA GGT GGA ATA GCT CCA    1440
           Val Ala Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro
           465                 470             475                 480
  35
           GCT ATC AGT CTG TCA GCT GCT GCT GGA ATT GGT GTT GAT GAC CTT CGT    1488
           Ala Ile Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg
                           485                 490             495

  40       CGC TTA TGC ATA CTC AGG ATG AGT TTT GTG AAA GGC TGG GGA CCG GAT    1536
           Arg Leu Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp
                       500                 505             510

           TAC CCA AGA CAG AGC ATC AAA GAA ACA CCT TGC TGG ATT GAA ATT CAC    1584
  45       Tyr Pro Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His
                       515                 520             525

           TTA CAC CGG GCC CTC CAG CTC CTA GAC GAA GTA CTT CAT ACC ATG CCG    1632
           Leu His Arg Ala Leu Gln Leu Leu Asp Glu Val Leu His Thr Met Pro
  50               530                 535             540

           ATT GCA GAC CCA CAA CCT TTA GAC TGG GAT CCA CCG GTC GCC ACC ATG    1680
           Ile Ala Asp Pro Gln Pro Leu Asp Trp Asp Pro Pro Val Ala Thr Met
           545                 550             555                 560
  55
           GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC    1728
```

174

175

```
          Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                          565                 570                 575

  5       GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG       1776
          Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
                          580                 585                 590

          GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC       1824
  10      Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
                          595                 600                 605

          ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG       1872
          Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
                          610                 615                 620
  15
          ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG       1920
          Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
          625                 630                 635                 640

  20      CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC       1968
          His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                          645                 650                 655

          ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG       2016
  25      Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
                          660                 665                 670

          AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC       2064
          Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
  30                      675                 680                 685

          GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC       2112
          Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
                          690                 695                 700
  35
          TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC       2160
          Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
          705                 710                 715                 720

  40      ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG       2208
          Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
                          725                 730                 735

          CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC       2256
  45      Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
                          740                 745                 750

          GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC       2304
          Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
  50                      755                 760                 765

          AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG       2352
          Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
                          770                 775                 780
  55
          ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA          2397
                                                                              175
```

```
Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
785                 790                 795
```

5   (2) INFORMATION FOR SEQ ID NO:77:

           (i) SEQUENCE CHARACTERISTICS:
              (A) LENGTH: 798 amino acids
              (B) TYPE: amino acid
10   (C) STRANDEDNESS: single
              (D) TOPOLOGY: linear

           (ii) MOLECULE TYPE: protein
           (v) FRAGMENT TYPE: internal
15

           (xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

```
     Met Asp Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys
      1               5               10              15
20   Leu Ser Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser
                  20              25              30
     Glu Thr Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys
          35              40              45
     Glu Lys Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn
25        50              55              60
     Gly Ala His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly
      65              70              75              80
     Arg Leu Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala
                  85              90              95
30   Arg Leu Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val
                  100             105             110
     Lys Tyr Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val
                  115             120             125
     Asn Pro Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser
35        130             135             140
     Gly Leu Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp
     145             150             155             160
     Glu Tyr Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly
                  165             170             175
40   His Ser Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr
                  180             185             190
     Glu Thr Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala
                  195             200             205
     Thr Ser Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln
45        210             215             220
     Pro Ala Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile
     225             230             235             240
     Ala Ser Gly Pro Gln Pro Gly Gln Gln Asn Gly Phe Thr Gly Gln
                  245             250             255
50   Pro Ala Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg
                  260             265             270
     Thr Ala Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu
                  275             280             285
     Gln His His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val
55        290             295             300
     His Asn Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Pro Ala Pro
```

```
        305                    310                    315                    320
        Glu Tyr Trp Cys Ser Ile Ala Tyr Phe Glu Met Asp Val Gln Val Gly
                         325                    330                    335
        Glu Thr Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly
  5                  340                    345                    350
        Tyr Val Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser
                     355                    360                    365
        Asn Val His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly
                 370                    375                    380
 10     Lys Gly Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg
        385                    390                    395                    400
        Cys Leu Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg
                     405                    410                    415
        Glu Ala Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser
 15                  420                    425                    430
        Ala Tyr Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln
                     435                    440                    445
        Gln Gln Ala Ala Thr Ala Gln Ala Ala Ala Ala Gln Ala Ala Ala
                 450                    455                    460
 20     Val Ala Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro
        465                    470                    475                    480
        Ala Ile Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg
                     485                    490                    495
        Arg Leu Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp
 25                  500                    505                    510
        Tyr Pro Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His
                     515                    520                    525
        Leu His Arg Ala Leu Gln Leu Leu Asp Glu Val Leu His Thr Met Pro
                 530                    535                    540
 30     Ile Ala Asp Pro Gln Pro Leu Asp Trp Asp Pro Pro Val Ala Thr Met
        545                    550                    555                    560
        Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                     565                    570                    575
        Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
 35                  580                    585                    590
        Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
                     595                    600                    605
        Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
                 610                    615                    620
 40     Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
        625                    630                    635                    640
        His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                     645                    650                    655
        Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
 45                  660                    665                    670
        Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
                     675                    680                    685
        Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
                 690                    695                    700
 50     Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
        705                    710                    715                    720
        Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
                     725                    730                    735
        Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
 55                  740                    745                    750
        Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
```

SUBSTITUTE SHEET (RULE 26)

```
          755                  760                  765
     Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
          770                  775                  780
     Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
5    785                  790                  795
```

     (2) INFORMATION FOR SEQ ID NO:78:

          (i) SEQUENCE CHARACTERISTICS:
10   (A) LENGTH: 3138 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: single
               (D) TOPOLOGY: linear

15   (ii) MOLECULE TYPE: cDNA
          (ix) FEATURE:

               (A) NAME/KEY: Coding Sequence
               (B) LOCATION: 1...3135
20   (D) OTHER INFORMATION:

          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

```
     ATG GCG GGC TGG ATC CAG GCC CAG CAG CTG CAG GGA GAC GCG CTG CGC    48
25   Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln Gly Asp Ala Leu Arg
      1               5                   10                  15

     CAG ATG CAG GTG CTG TAC GGC CAG CAC TTC CCC ATC GAG GTC CGG CAC    96
     Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro Ile Glu Val Arg His
30                   20                  25                  30

     TAC TTG GCC CAG TGG ATT GAG AGC CAG CCA TGG GAT GCC ATT GAC TTG   144
     Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp Asp Ala Ile Asp Leu
                     35                  40                  45
35
     GAC AAT CCC CAG GAC AGA GCC CAA GCC ACC CAG CTC CTG GAG GGC CTG   192
     Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln Leu Leu Glu Gly Leu
                 50                  55                  60

40   GTG CAG GAG CTG CAG AAG AAG GCG GAG CAC CAG GTG GGG GAA GAT GGG   240
     Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln Val Gly Glu Asp Gly
     65                  70                  75                  80

     TTT TTA CTG AAG ATC AAG CTG GGG CAC TAC GCC ACG CAG CTC CAG AAA   288
45   Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala Thr Gln Leu Gln Lys
                         85                  90                  95

     ACA TAT GAC CGC TGC CCC CTG GAG CTG GTC CGC TGC ATC CGG CAC ATT   336
     Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg Cys Ile Arg His Ile
50                   100                 105                 110

     CTG TAC AAT GAA CAG AGG CTG GTC CGA GAA GCC AAC AAT TGC AGC TCT   384
     Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala Asn Asn Cys Ser Ser
                     115                 120                 125
55
     CCG GCT GGG ATC CTG GTT GAC GCC ATG TCC CAG AAG CAC CTT CAG ATC   432
```

```
           Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln Lys His Leu Gln Ile
               130                 135                 140

  5        AAC CAG ACA TTT GAG GAG CTG CGA CTG GTC ACG CAG GAC ACA GAG AAT    480
           Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr Gln Asp Thr Glu Asn
               145                 150                 155                 160

           GAG CTG AAG AAA CTG CAG CAG ACT CAG GAG TAC TTC ATC ATC CAG TAC    528
 10        Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr Phe Ile Ile Gln Tyr
                           165                 170                 175

           CAG GAG AGC CTG AGG ATC CAA GCT CAG TTT GCC CAG CTG GCC CAG CTG    576
           Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala Gln Leu Ala Gln Leu
 15                        180                 185                 190

           AGC CCC CAG GAG CGT CTG AGC CGG GAG ACG GCC CTC CAG CAG AAG CAG    624
           Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala Leu Gln Gln Lys Gln
                           195                 200                 205

 20        GTG TCT CTG GAG GCC TGG TTG CAG CGT GAG GCA CAG ACA CTG CAG CAG    672
           Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala Gln Thr Leu Gln Gln
                       210                 215                 220

           TAC CGC GTG GAG CTG GCC GAG AAG CAC CAG AAG ACC CTG CAG CTG CTG    720
 25        Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys Thr Leu Gln Leu Leu
           225                 230                 235                 240

           CGG AAG CAG CAG ACC ATC ATC CTG GAT GAC GAG CTG ATC CAG TGG AAG    768
           Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu Leu Ile Gln Trp Lys
 30                        245                 250                 255

           CGG CGG CAG CAG CTG GCC GGG AAC GGC GGG CCC CCC GAG GGC AGC CTG    816
           Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro Pro Glu Gly Ser Leu
                           260                 265                 270
 35
           GAC GTG CTA CAG TCC TGG TGT GAG AAG TTG GCC GAG ATC ATC TGG CAG    864
           Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala Glu Ile Ile Trp Gln
                       275                 280                 285

 40        AAC CGG CAG CAG ATC CGC AGG GCT GAG CAC CTC TGC CAG CAG CTG CCC    912
           Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu Cys Gln Gln Leu Pro
                       290                 295                 300

           ATC CCC GGC CCA GTG GAG GAG ATG CTG GCC GAG GTC AAC GCC ACC ATC    960
 45        Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu Val Asn Ala Thr Ile
           305                 310                 315                 320

           ACG GAC ATT ATC TCA GCC CTG GTG ACC AGC ACA TTC ATC ATT GAG AAG    1008
           Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr Phe Ile Ile Glu Lys
 50                        325                 330                 335

           CAG CCT CCT CAG GTC CTG AAG ACC CAG ACC AAG TTT GCA GCC ACC GTA    1056
           Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys Phe Ala Ala Thr Val
                           340                 345                 350
 55
           CGC CTG CTG GTG GGC GGG AAG CTG AAC GTG CAC ATG AAT CCC CCC CAG    1104
```

179

180

```
      Arg Leu Leu Val Gly Gly Lys Leu Asn Val His Met Asn Pro Pro Gln
          355                 360             365

 5    GTG AAG GCC ACC ATC ATC AGT GAG CAG CAG GCC AAG TCT CTG CTT AAA        1152
      Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala Lys Ser Leu Leu Lys
          370                 375             380

      AAT GAG AAC ACC CGC AAC GAG TGC AGT GGT GAG ATC CTG AAC AAC TGC        1200
      Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu Ile Leu Asn Asn Cys
10    385                 390             395                 400

      TGC GTG ATG GAG TAC CAC CAA GCC ACG GGC ACC CTC AGT GCC CAC TTC        1248
      Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr Leu Ser Ala His Phe
                      405                 410             415
15
      AGG AAC ATG TCA CTG AAG AGG ATC AAG CGT GCT GAC CGG CGG GGT GCA        1296
      Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala Asp Arg Arg Gly Ala
                  420                 425             430

20    GAG TCC GTG ACA GAG GAG AAG TTC ACA GTC CTG TTT GAG TCT CAG TTC        1344
      Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu Phe Glu Ser Gln Phe
                  435                 440             445

      AGT GTT GGC AGC AAT GAG CTT GTG TTC CAG GTG AAG ACT CTG TCC CTA        1392
25    Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val Lys Thr Leu Ser Leu
                  450                 455             460

      CCT GTG GTT GTC ATC GTC CAC GGC AGC CAG GAC CAC AAT GCC ACG GCT        1440
      Pro Val Val Val Ile Val His Gly Ser Gln Asp His Asn Ala Thr Ala
30 .  465                 470                 475                 480

      ACT GTG CTG TGG GAC AAT GCC TTT GCT GAG CCG GGC AGG GTG CCA TTT        1488
      Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro Gly Arg Val Pro Phe
                      485                 490                 495
35
      GCC GTG CCT GAC AAA GTG CTG TGG CCG CAG CTG TGT GAG GCG CTC AAC        1536
      Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu Cys Glu Ala Leu Asn
                  500                 505             510

40    ATG AAA TTC AAG GCC GAA GTG CAG AGC AAC CGG GGC CTG ACC AAG GAG        1584
      Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg Gly Leu Thr Lys Glu
                  515                 520             525

      AAC CTC GTG TTC CTG GCG CAG AAA CTG TTC AAC AAC AGC AGC AGC CAC        1632
45    Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn Asn Ser Ser Ser His
                  530                 535             540

      CTG GAG GAC TAC AGT GGC CTG TCC GTG TCC TGG TCC CAG TTC AAC AGG        1680
      Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp Ser Gln Phe Asn Arg
50    545                 550                 555                 560

      GAG AAC TTG CCG GGC TGG AAC TAC ACC TTC TGG CAG TGG TTT GAC GGG        1728
      Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp Gln Trp Phe Asp Gly
                      565                 570                 575
55
      GTG ATG GAG GTG TTG AAG AAG CAC CAC AAG CCC CAC TGG AAT GAT GGG        1776
```

180

181

```
           Val Met Glu Val Leu Lys Lys His His Lys Pro His Trp Asn Asp Gly
                       580               585               590

  5        GCC ATC CTA GGT TTT GTG AAT AAG CAA CAG GCC CAC GAC CTG CTC ATC     1824
           Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala His Asp Leu Leu Ile
                       595               600               605

           AAC AAG CCC GAC GGG ACC TTC TTG TTG CGC TTT AGT GAC TCA GAA ATC     1872
           Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe Ser Asp Ser Glu Ile
 10            610               615               620

           GGG GGC ATC ACC ATC GCC TGG AAG TTT GAC TCC CCG GAA CGC AAC CTG     1920
           Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser Pro Glu Arg Asn Leu
           625               630               635               640
 15
           TGG AAC CTG AAA CCA TTC ACC ACG CGG GAT TTC TCC ATC AGG TCC CTG     1968
           Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe Ser Ile Arg Ser Leu
                           645               650               655

 20        GCT GAC CGG CTG GGG GAC CTG AGC TAT CTC ATC TAT GTG TTT CCT GAC     2016
           Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile Tyr Val Phe Pro Asp
                       660               665               670

           CGC CCC AAG GAT GAG GTC TTC TCC AAG TAC TAC ACT CCT GTG CTG GCT     2064
 25        Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr Thr Pro Val Leu Ala
                       675               680               685

           AAA GCT GTT GAT GGA TAT GTG AAA CCA CAG ATC AAG CAA GTG GTC CCT     2112
           Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile Lys Gln Val Val Pro
 30            690               695               700

           GAG TTT GTG AAT GCA TCT GCA GAT GCT GGG GGC AGC AGC GCC ACG TAC     2160
           Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly Ser Ser Ala Thr Tyr
           705               710               715               720
 35
           ATG GAC CAG GCC CCC TCC CCA GCT GTG TGC CCC CAG GCT CCC TAT AAC     2208
           Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro Gln Ala Pro Tyr Asn
                           725               730               735

 40        ATG TAC CCA CAG AAC CCT GAC CAT GTA CTC GAT CAG GAT GGA GAA TTC     2256
           Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp Gln Asp Gly Glu Phe
                       740               745               750

           GAC CTG GAT GAG ACC ATG GAT GTG GCC AGG CAC GTG GAG GAA CTC TTA     2304
 45        Asp Leu Asp Glu Thr Met Asp Val Ala Arg His Val Glu Glu Leu Leu
                       755               760               765

           CGC CGA CCA ATG GAC AGT CTT GAC TCC CGC CTC TCG CCC CCT GCC GGT     2352
           Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu Ser Pro Pro Ala Gly
 50            770               775               780

           CTT TTC ACC TCT GCC AGA GGC TCC CTC TCA TGG GTA CCG CGG GCC CGG     2400
           Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser Trp Val Pro Arg Ala Arg
           785               790               795               800
 55
           GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC     2448
```

181

182

```
           Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr
                           805                 810                 815

    5      GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC    2496
           Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His
                           820                 825                 830

           AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG    2544
   10      Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys
                           835                 840                 845

           CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG    2592
           Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp
                       850                 855                 860
   15
           CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC    2640
           Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg
           865                 870                 875                 880

   20      TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC    2688
           Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro
                               885                 890                 895

           GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC    2736
   25      Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn
                           900                 905                 910

           TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC    2784
           Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn
   30                  915                 920                 925

           CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG    2832
           Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu
                       930                 935                 940
   35
           GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG    2880
           Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met
           945                 950                 955                 960

   40      GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC    2928
           Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
                               965                 970                 975

           AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC    2976
   45      Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
                           980                 985                 990

           ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG    3024
           Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
   50                  995                 1000                1005

           AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC    3072
           Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
                       1010                1015                1020
   55
           ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG    3120
```

182

183

```
    Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
    1025                1030                1035                1040


    GAC GAG CTG TAC AAG TAA                                       3138
5   Asp Glu Leu Tyr Lys
                    1045



            (2) INFORMATION FOR SEQ ID NO:79:
10

            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 1045 amino acids
                (B) TYPE: amino acid
                (C) STRANDEDNESS: single
15              (D) TOPOLOGY: linear


            (ii) MOLECULE TYPE: protein
            (v) FRAGMENT TYPE: internal


20          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:


    Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln Gly Asp Ala Leu Arg
    1               5                   10                  15
    Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro Ile Glu Val Arg His
25                  20                  25                  30
    Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp Asp Ala Ile Asp Leu
                35                  40                  45
    Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln Leu·Leu Glu Gly Leu
                50                  55                  60
30  Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln Val Gly Glu Asp Gly
    65                  70                  75                  80
    Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala Thr Gln Leu Gln Lys
                    85                  90                  95
    Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg Cys Ile Arg His Ile
35                  100                 105                 110
    Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala Asn Asn Cys Ser Ser
                115                 120                 125
    Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln Lys His Leu Gln Ile
                130                 135                 140
40  Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr Gln Asp Thr Glu Asn
    145                 150                 155                 160
    Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr Phe Ile Ile Gln Tyr
                    165                 170                 175
    Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala Gln Leu Ala Gln Leu
45                  180                 185                 190
    Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala Leu Gln Gln Lys Gln
                195                 200                 205
    Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala Gln Thr Leu Gln Gln
                210                 215                 220
50  Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys Thr Leu Gln Leu Leu
    225                 230                 235                 240
    Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu Leu Ile Gln Trp Lys
                    245                 250                 255
    Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro Pro Glu Gly Ser Leu
55                  260                 265                 270
    Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala Glu Ile Ile Trp Gln
```

```
              275                    280                    285
      Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu Cys Gln Gln Leu Pro
          290                    295                    300
      Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu Val Asn Ala Thr Ile
  5   305                    310                    315                    320
      Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr Phe Ile Ile Glu Lys
                         325                    330                    335
      Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys Phe Ala Ala Thr Val
                     340                    345                    350
 10   Arg Leu Leu Val Gly Gly Lys Leu Asn Val His Met Asn Pro Pro Gln
                     355                    360                    365
      Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala Lys Ser Leu Leu Lys
          370                    375                    380
      Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu Ile Leu Asn Asn Cys
 15   385                    390                    395                    400
      Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr Leu Ser Ala His Phe
                         405                    410                    415
      Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala Asp Arg Arg Gly Ala
                     420                    425                    430
 20   Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu Phe Glu Ser Gln Phe
                     435                    440                    445
      Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val Lys Thr Leu Ser Leu
          450                    455                    460
      Pro Val Val Val Ile Val His Gly Ser Gln Asp His Asn Ala Thr Ala
·25   465                    470                    475                    480
      Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro Gly Arg Val Pro Phe
                         485                    490                    495
      Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu Cys Glu Ala Leu Asn
                     500                    505                    510
 30   Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg Gly Leu Thr Lys Glu
                     515                    520                    525
      Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn Asn Ser Ser Ser His
          530                    535                    540
      Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp Ser Gln Phe Asn Arg
 35   545                    550                    555                    560
      Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp Gln Trp Phe Asp Gly
                     565                    570                    575
      Val Met Glu Val Leu Lys Lys His His Lys Pro His Trp Asn Asp Gly
                     580                    585                    590
 40   Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala His Asp Leu Leu Ile
                     595                    600                    605
      Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe Ser Asp Ser Glu Ile
          610                    615                    620
      Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser Pro Glu Arg Asn Leu
 45   625                    630                    635                    640
      Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe Ser Ile Arg Ser Leu
                     645                    650                    655
      Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile Tyr Val Phe Pro Asp
                     660                    665                    670
 50   Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr Thr Pro Val Leu Ala
                     675                    680                    685
      Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile Lys Gln Val Val Pro
          690                    695                    700
      Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly Ser Ser Ala Thr Tyr
 55   705                    710                    715                    720
      Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro Gln Ala Pro Tyr Asn
```

185

```
                    725               730               735
      Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp Gln Asp Gly Glu Phe
                    740               745               750
 5    Asp Leu Asp Glu Thr Met Asp Val Ala Arg His Val Glu Glu Leu Leu
                    755               760               765
      Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu Ser Pro Pro Ala Gly
                    770               775               780
      Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser Trp Val Pro Arg Ala Arg
      785               790               795               800
10    Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr
                        805               810               815
      Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His
                    820               825               830
      Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys
15                835               840               845
      Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp
          850               855               860
      Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg
      865               870               875               880
20    Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro
                    885               890               895
      Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn
                    900               905               910
      Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn
25                915               920               925
      Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu
          930               935               940
      Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met
      945               950               955               960
30    Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
                    965               970               975
      Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
                    980               985               990
      Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
35            995               1000              1005
      Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
          1010              1015              1020
      Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
      025               1030              1035              1040
40    Asp Glu Leu Tyr Lys
                    1045
```

(2) INFORMATION FOR SEQ ID NO:80:

45   (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 28 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear
50

          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

      TGGGATCCTC AGGCCGTGCT GCTGGCCG   28
55
          (2) INFORMATION FOR SEQ ID NO:81:

BNSDOCID: <WO___9845704A2_I_>

        (i) SEQUENCE CHARACTERISTICS:
           (A) LENGTH: 27 base pairs
           (B) TYPE: nucleic acid
5   (C) STRANDEDNESS: single
           (D) TOPOLOGY: linear

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:
10

GTCTCGAGGG AGCATGGGCA CCTTGCG   27

        (2) INFORMATION FOR SEQ ID NO:82:

15   (i) SEQUENCE CHARACTERISTICS:
           (A) LENGTH: 27 base pairs
           (B) TYPE: nucleic acid
           (C) STRANDEDNESS: single
           (D) TOPOLOGY: linear
20

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

TGGGATCCGA GAAGTCTATA TCCCATC   27
25

        (2) INFORMATION FOR SEQ ID NO:83:

        (i) SEQUENCE CHARACTERISTICS:
           (A) LENGTH: 28 base pairs
30   (B) TYPE: nucleic acid
           (C) STRANDEDNESS: single
           (D) TOPOLOGY: linear

35   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

TGGGATCCTT AGAAGTCTAT ATCCCATC   28

        (2) INFORMATION FOR SEQ ID NO:84:
40
        (i) SEQUENCE CHARACTERISTICS:
           (A) LENGTH: 28 base pairs
           (B) TYPE: nucleic acid
           (C) STRANDEDNESS: single
45   (D) TOPOLOGY: linear

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

50   GTCTCGAGCC ATGAACGCCC CCGAGCGG   28

        (2) INFORMATION FOR SEQ ID NO:85:

        (i) SEQUENCE CHARACTERISTICS:
55   (A) LENGTH: 30 base pairs
           (B) TYPE: nucleic acid

```
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear


5         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

   GTGAATTCTC GTCTGATTTC TGGCAGGAGG                                    30

          (2) INFORMATION FOR SEQ ID NO:86:
10
          (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 30 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
15        (D) TOPOLOGY: linear



          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

20 GTGAATTCTT TACGTCTGAT TTCTGGCAGG                                    30

          (2) INFORMATION FOR SEQ ID NO:87:


          (i) SEQUENCE CHARACTERISTICS:
25        (A) LENGTH: 34 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear


30
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

   GTCTCGAGCC ATGGACGAAC TGTTCCCCCT CATC                               34

35        (2) INFORMATION FOR SEQ ID NO:88:


          (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 31 base pairs
          (B) TYPE: nucleic acid
40        (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear


          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:
45
   GTGGATCCAA GGAGCTGATC TGACTCAGCA G                                  31

          (2) INFORMATION FOR SEQ ID NO:89:


50        (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 32 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear
55
```

SUBSTITUTE SHEET (RULE 26)

188

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

GTGGATCCTT AGGAGCTGAT CTGACTCAGC AG   32

5   (2) INFORMATION FOR SEQ ID NO:90:

           (i) SEQUENCE CHARACTERISTICS:
             (A) LENGTH: 32 base pairs
             (B) TYPE: nucleic acid
10   (C) STRANDEDNESS: single
             (D) TOPOLOGY: linear

           (xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:
15
CCTCCTAAGC TTATCATGGA CCATTATGAT TC   32

           (2) INFORMATION FOR SEQ ID NO:91:

20   (i) SEQUENCE CHARACTERISTICS:
             (A) LENGTH: 33 base pairs
             (B) TYPE: nucleic acid
             (C) STRANDEDNESS: single
             (D) TOPOLOGY: linear
25

           (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

CCTCCTGGAT CCCTGCGCAG GATGATGGTC CAG   33
30
           (2) INFORMATION FOR SEQ ID NO:92:

           (i) SEQUENCE CHARACTERISTICS:
             (A) LENGTH: 45 base pairs
35   (B) TYPE: nucleic acid
             (C) STRANDEDNESS: single
             (D) TOPOLOGY: linear

40   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

GGATGGAAGC TTCAATGGCT GCCATCCGGA AGAAACTGGT GATTG   45

           (2) INFORMATION FOR SEQ ID NO:93:
45
           (i) SEQUENCE CHARACTERISTICS:
             (A) LENGTH: 45 base pairs
             (B) TYPE: nucleic acid
             (C) STRANDEDNESS: single
50   (D) TOPOLOGY: linear

           (xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

55   GGATGGGGAT CCTCACAAGA CAAGGCAACC AGATTTTTTC TTCCC   45

BNSDOCID <WO___9845704A2_L_>

(2) INFORMATION FOR SEQ ID NO:94:

    (i) SEQUENCE CHARACTERISTICS:
      (A) LENGTH: 29 base pairs
5   (B) TYPE: nucleic acid
      (C) STRANDEDNESS: single
      (D) TOPOLOGY: linear

10   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

GGGAAGCTTC CATGAGCGAG ACGGTCATC   29

      (2) INFORMATION FOR SEQ ID NO:95:
15
    (i) SEQUENCE CHARACTERISTICS:
      (A) LENGTH: 28 base pairs
      (B) TYPE: nucleic acid
      (C) STRANDEDNESS: single
20   (D) TOPOLOGY: linear

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

25 CCCGGATCCT CAGGGAGAAC CCCGCTTC   28

      (2) INFORMATION FOR SEQ ID NO:96:

    (i) SEQUENCE CHARACTERISTICS:
30   (A) LENGTH: 30 base pairs
      (B) TYPE: nucleic acid
      (C) STRANDEDNESS: single
      (D) TOPOLOGY: linear

35
      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

GTGAATTCGA CCATGGAGCG GCCCCCGGGG   30

40   (2) INFORMATION FOR SEQ ID NO:97:

    (i) SEQUENCE CHARACTERISTICS:
      (A) LENGTH: 27 base pairs
      (B) TYPE: nucleic acid
45   (C) STRANDEDNESS: single
      (D) TOPOLOGY: linear

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:
50
GTGGTACCCA TTCTGTTAAC CAACTCC   27

      (2) INFORMATION FOR SEQ ID NO:98:

55   (i) SEQUENCE CHARACTERISTICS:
      (A) LENGTH: 28 base pairs

190

```
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear


5

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:


GTGGTACCTC ATTCTGTTAA CCAACTCC                                    28

10          (2) INFORMATION FOR SEQ ID NO:99:


        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 28 base pairs
            (B) TYPE: nucleic acid
15          (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear



        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:
20

GTCTCGAGAG ATGCTGTCCC GTGGGTGG                                    28


            (2) INFORMATION FOR SEQ ID NO:100:


25      (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 27 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear
30

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:


GTGAATTCGC TTCCTCTTGA GGGAACC                                     27
35          (2) INFORMATION FOR SEQ ID NO:101:


        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 27 base pairs
40          (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear



45      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:


GTGAATTCAC TTCCTCTTGA GGGAACC                                     27

            (2) INFORMATION FOR SEQ ID NO:102:
50

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 29 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
55          (D) TOPOLOGY: linear
```

190

SUBSTITUTE SHEET (RULE 26)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

GTCTCGAGCC ATGGAGAACT TCCAAAAGG   29

   (2) INFORMATION FOR SEQ ID NO:103:

   (i) SEQUENCE CHARACTERISTICS:
     (A) LENGTH: 28 base pairs
     (B) TYPE: nucleic acid
     (C) STRANDEDNESS: single
     (D) TOPOLOGY: linear

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

GTGGATCCCA GAGTCGAAGA TGGGGTAC   28

      (2) INFORMATION FOR SEQ ID NO:104:

   (i) SEQUENCE CHARACTERISTICS:
     (A) LENGTH: 29 base pairs
     (B) TYPE: nucleic acid
     (C) STRANDEDNESS: single
     (D) TOPOLOGY: linear

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

GTGGATCCTC AGAGTCGAAG ATGGGGTAC   29

      (2) INFORMATION FOR SEQ ID NO:105:

   (i) SEQUENCE CHARACTERISTICS:
     (A) LENGTH: 30 base pairs
     (B) TYPE: nucleic acid
     (C) STRANDEDNESS: single
     (D) TOPOLOGY: linear

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

GTGAATTCGG CGATGCCAGA CCCCGCGGCG   30

      (2) INFORMATION FOR SEQ ID NO:106:

   (i) SEQUENCE CHARACTERISTICS:
     (A) LENGTH: 32 base pairs
     (B) TYPE: nucleic acid
     (C) STRANDEDNESS: single
     (D) TOPOLOGY: linear

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

GTGGATCCCA GGCACAGGCA GCCTCAGCCT TC   32

192

(2) INFORMATION FOR SEQ ID NO:107:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 33 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

GTGGATCCTC AGGCACAGGC AGCCTCAGCC TTC   33

    (2) INFORMATION FOR SEQ ID NO:108:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 2616 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA
    (ix) FEATURE:

       (A) NAME/KEY: Coding Sequence
       (B) LOCATION: 1...2613
       (D) OTHER INFORMATION:

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
             20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
         35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
     50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                 85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
```

```
        Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100                 105                 110

 5      GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC    384
        Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                    115                 120                 125

        ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC    432
        Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
10          130                 135                 140

        AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC    480
        Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
        145                 150                 155                 160
15
        GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC    528
        Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                        165                 170                 175

20      GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC    576
        Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                        180                 185                 190

        CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
25      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                    195                 200                 205

        AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
        Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
30          210                 215                 220

        GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
        Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
        225                 230                 235                 240
35
        GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG GCG ATG CCA GAC CCC    768
        Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ala Met Pro Asp Pro
                        245                 250                 255

40      GCG GCG CAC CTG CCC TTC TTC TAC GGC AGC ATC TCG CGT GCC GAG GCC    816
        Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser Arg Ala Glu Ala
                    260                 265                 270

        GAG GAG CAC CTG AAG CTG GCG GGC ATG GCG GAC GGG CTC TTC CTG CTG    864
45      Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly Leu Phe Leu Leu
                    275                 280                 285

        CGC CAG TGC CTG CGC TCG CTG GGC GGC TAT GTG CTG TCG CTC GTG CAC    912
        Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu Ser Leu Val His
50          290                 295                 300

        GAT GTG CGC TTC CAC CAC TTT CCC ATC GAG CGC CAG CTC AAC GGC ACC    960
        Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln Leu Asn Gly Thr
        305                 310                 315                 320
55
        TAC GCC ATT GCC GGC GGC AAA GCG CAC TGT GGA CCG GCA GAG CTC TGC   1008
```

193

194

```
                    Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro Ala Glu Leu Cys
                                    325             330             335

  5   GAG TTC TAC TCG CGC GAC CCC GAC GGG CTG CCC TGC AAC CTG CGC AAG   1056
      Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys Asn Leu Arg Lys
                    340             345             350

      CCG TGC AAC CGG CCG TCG GGC CTC GAG CCG CAG CCG GGG GTC TTC GAC   1104
      Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro Gly Val Phe Asp
 10                 355             360             365

      TGC CTG CGA GAC GCC ATG GTG CGT GAC TAC GTG CGC CAG ACG TGG AAG   1152
      Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg Gln Thr Trp Lys
                    370             375             380
 15
      CTG GAG GGC GAG GCC CTG GAG CAG GCC ATC ATC AGC CAG GCC CCG CAG   1200
      Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser Gln Ala Pro Gln
      385                 390             395             400

 20   GTG GAG AAG CTC ATT GCT ACG ACG GCC CAC GAG CGG ATG CCC TGG TAC   1248
      Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg Met Pro Trp Tyr
                        405             410             415

      CAC AGC AGC CTG ACG CGT GAG GAG GCC GAG CGC AAA CTT TAC TCT GGG   1296
 25   His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys Leu Tyr Ser Gly
                    420             425             430

      GCG CAG ACC GAC GGC AAG TTC CTG CTG AGG CCG CGG AAG GAG CAG GGC   1344
      Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg Lys Glu Gln Gly
 30                 435             440             445

      ACA TAC GCC CTG TCC CTC ATC TAT GGG AAG ACG GTG TAC CAC TAC CTC   1392
      Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val Tyr His Tyr Leu
                    450             455             460
 35
      ATC AGC CAA GAC AAG GCG GGC AAG TAC TGC ATT CCC GAG GGC ACC AAG   1440
      Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro Glu Gly Thr Lys
      465                 470             475             480

 40   TTT GAC ACG CTC TGG CAG CTG GTG GAG TAT CTG AAG CTG AAG GCG GAC   1488
      Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys Leu Lys Ala Asp
                        485             490             495

      GGG CTC ATC TAC TGC CTG AAG GAG GCC TGC CCC AAC AGC AGT GCC AGC   1536
 45   Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn Ser Ser Ala Ser
                    500             505             510

      AAC GCC TCA GGG GCT GCT GCT CCC ACA CTC CCA GCC CAC CCA TCC ACG   1584
      Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala His Pro Ser Thr
 50                 515             520             525

      TTG ACT CAT CCT CAG AGA CGA ATC GAC ACC CTC AAC TCA GAT GGA TAC   1632
      Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn Ser Asp Gly Tyr
                    530             535             540
 55
      ACC CCT GAG CCA GCA CGC ATA ACG TCC CCA GAC AAA CCG CGG CCG ATG   1680
```

194

```
          Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys Pro Arg Pro Met
          545                 550                 555                 560

   5      CCC ATG GAC ACG AGC GTG TAT GAG AGC CCC TAC AGC GAC CCA GAG GAG   1728
          Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser Asp Pro Glu Glu
                              565                 570                 575

  10      CTC AAG GAC AAG AAG CTC TTC CTG AAG CGC GAT AAC CTC CTC ATA GCT   1776
          Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn Leu Leu Ile Ala
                      580                 585                 590

          GAC ATT GAA CTT GGC TGC GGC AAC TTT GGC TCA GTG CGC CAG GGC GTG   1824
          Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val Arg Gln Gly Val
                          595                 600                 605
  15

          TAC CGC ATG CGC AAG AAG CAG ATC GAC GTG GCC ATC AAG GTG CTG AAG   1872
          Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile Lys Val Leu Lys
                  610                 615                 620

  20      CAG GGC ACG GAG AAG GCA GAC ACG GAA GAG ATG ATG CGC GAG GCG CAG   1920
          Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met Arg Glu Ala Gln
          625                 630                 635                 640

          ATC ATG CAC CAG CTG GAC AAC CCC TAC ATC GTG CGG CTC ATT GGC GTC   1968
  25      Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg Leu Ile Gly Val
                              645                 650                 655

          TGC CAG GCC GAG GCC CTC ATG CTG GTC ATG GAG ATG GCT GGG GGC GGG   2016
          Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met Ala Gly Gly Gly
  30                      660                 665                 670

          CCG CTG CAC AAG TTC CTG GTC GGC AAG AGG GAG GAG ATC CCT GTG AGC   2064
          Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu Ile Pro Val Ser
                      675                 680                 685
  35
          AAT GTG GCC GAG CTG CTG CAC CAG GTG TCC ATG GGG ATG AAG TAC CTG   2112
          Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly Met Lys Tyr Leu
                  690                 695                 700

  40      GAG GAG AAG AAC TTT GTG CAC CGT GAC CTG GCG GCC CGC AAC GTC CTG   2160
          Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu
          705                 710                 715                 720

          CTG GTT AAC CGG CAC TAC GCC AAG ATC AGC GAC TTT GGC CTC TCC AAA   2208
  45      Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe Gly Leu Ser Lys
                          725                 730                 735

          GCA CTG GGT GCC GAC GAC AGC TAC TAC ACT GCC CGC TCA GCA GGG AAG   2256
          Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg Ser Ala Gly Lys
  50                      740                 745                 750

          TGG CCG CTC AAG TGG TAC GCA CCC GAA TGC ATC AAC TTC CGC AAG TTC   2304
          Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn Phe Arg Lys Phe
                      755                 760                 765
  55
          TCC AGC CGC AGC GAT GTC TGG AGC TAT GGG GTC ACC ATG TGG GAG GCC   2352
```

SUBSTITUTE SHEET (RULE 26)

```
           Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr Met Trp Glu Ala
               770                 775                 780

  5        TTG TCC TAC GGC CAG AAG CCC TAC AAG AAG ATG AAA GGG CCG GAG GTC      2400
           Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys Gly Pro Glu Val
           785                 790                 795                 800

           ATG GCC TTC ATC GAG CAG GGC AAG CGG ATG GAG TGC CCA CCA GAG TGT      2448
           Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys Pro Pro Glu Cys
 10                        805                 810                 815

           CCA CCC GAA CTG TAC GCA CTC ATG AGT GAC TGC TGG ATC TAC AAG TGG      2496
           Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp Ile Tyr Lys Trp
                       820                 825                 830
 15
           GAG GAT CGC CCC GAC TTC CTG ACC GTG GAG CAG CGC ATG CGA GCC TGT      2544
           Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg Met Arg Ala Cys
                       835                 840                 845

 20        TAC TAC AGC CTG GCC AGC AAG GTG GAA GGG CCC CCA GGC AGC ACA CAG      2592
           Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro Gly Ser Thr Gln
                       850                 855                 860

           AAG GCT GAG GCT GCC TGT GCC TGA                                      2616
 25        Lys Ala Glu Ala Ala Cys Ala
           865                 870


                   (2) INFORMATION FOR SEQ ID NO:109:
 30
                       (i) SEQUENCE CHARACTERISTICS:
                           (A) LENGTH: 871 amino acids
                           (B) TYPE: amino acid
                           (C) STRANDEDNESS: single
 35                        (D) TOPOLOGY: linear

                       (ii) MOLECULE TYPE: protein
                       (v) FRAGMENT TYPE: internal

 40                    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

           Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
            1               5                  10                 15
           Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 45                    20                  25                 30
           Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                       35                  40                 45
           Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                       50                  55                 60
 50        Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
           65                  70                  75                 80
           Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                           85                  90                 95
           Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
 55                        100                 105                110
           Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
```

```
                    115                   120                   125
        Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
            130                   135                   140
        Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
 5      145                   150                   155                   160
        Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                        165                   170                   175
        Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                        180                   185                   190
10      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                    195                   200                   205
        Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
            210                   215                   220
        Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
15      225                   230                   235                   240
        Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ala Met Pro Asp Pro
                        245                   250                   255
        Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser Arg Ala Glu Ala
                        260                   265                   270
20      Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly Leu Phe Leu Leu
                    275                   280                   285
        Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu Ser Leu Val His
            290                   295                   300
        Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln Leu Asn Gly Thr
25      305                   310                   315                   320
        Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro Ala Glu Leu Cys
                        325                   330                   335
        Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys Asn Leu Arg Lys
                        340                   345                   350
30      Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro Gly Val Phe Asp
                    355                   360                   365
        Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg Gln Thr Trp Lys
            370                   375                   380
        Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser Gln Ala Pro Gln
35      385                   390                   395                   400
        Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg Met Pro Trp Tyr
                        405                   410                   415
        His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys Leu Tyr Ser Gly
                        420                   425                   430
40      Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg Lys Glu Gln Gly
                    435                   440                   445
        Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val Tyr His Tyr Leu
                    450                   455                   460
        Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro Glu Gly Thr Lys
45      465                   470                   475                   480
        Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys Leu Lys Ala Asp
                        485                   490                   495
        Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn Ser Ser Ala Ser
                        500                   505                   510
50      Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala His Pro Ser Thr
                    515                   520                   525
        Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn Ser Asp Gly Tyr
                    530                   535                   540
        Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys Pro Arg Pro Met
55      545                   550                   555                   560
        Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser Asp Pro Glu Glu
```

197

```
                        565                   570                   575
        Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn Leu Leu Ile Ala
                    580                   585                   590
        Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val Arg Gln Gly Val
   5            595                   600                   605
        Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile Lys Val Leu Lys
            610                   615                   620
        Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met Arg Glu Ala Gln
        625                   630                   635                   640
  10    Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg Leu Ile Gly Val
                    645                   650                   655
        Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met Ala Gly Gly Gly
                    660                   665                   670
        Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu Ile Pro Val Ser
  15            675                   680                   685
        Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly Met Lys Tyr Leu
            690                   695                   700
        Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu
        705                   710                   715                   720
  20    Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe Gly Leu Ser Lys
                    725                   730                   735
        Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg Ser Ala Gly Lys
                    740                   745                   750
        Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn Phe Arg Lys Phe
  25            755                   760                   765
        Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr Met Trp Glu Ala
                    770                   775                   780
        Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys Gly Pro Glu Val
        785                   790                   795                   800
  30    Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys Pro Pro Glu Cys
                    805                   810                   815
        Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp Ile Tyr Lys Trp
                    820                   825                   830
        Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg Met Arg Ala Cys
  35            835                   840                   845
        Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro Gly Ser Thr Gln
            850                   855                   860
        Lys Ala Glu Ala Ala Cys Ala
        865                   870
```

  40

              (2) INFORMATION FOR SEQ ID NO:110:

              (i) SEQUENCE CHARACTERISTICS:
                   (A) LENGTH: 2598 base pairs
  45   (B) TYPE: nucleic acid
                   (C) STRANDEDNESS: single
                   (D) TOPOLOGY: linear

              (ii) MOLECULE TYPE: cDNA
  50   (ix) FEATURE:

                   (A) NAME/KEY: Coding Sequence
                   (B) LOCATION: 1...2595
                   (D) OTHER INFORMATION:
  55
              (xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

BNSDOCID: <WO___9845704A2_I_>

```
     ATG CCA GAC CCC GCG GCG CAC CTG CCC TTC TTC TAC GGC AGC ATC TCG        48
     Met Pro Asp Pro Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser
      1           5                   10                  15
 5

     CGT GCC GAG GCC GAG GAG CAC CTG AAG CTG GCG GGC ATG GCG GAC GGG        96
     Arg Ala Glu Ala Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly
                  20                  25                  30

10   CTC TTC CTG CTG CGC CAG TGC CTG CGC TCG CTG GGC GGC TAT GTG CTG       144
     Leu Phe Leu Leu Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu
              35                  40                  45

     TCG CTC GTG CAC GAT GTG CGC TTC CAC CAC TTT CCC ATC GAG CGC CAG       192
15   Ser Leu Val His Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln
              50                  55                  60

     CTC AAC GGC ACC TAC GCC ATT GCC GGC GGC AAA GCG CAC TGT GGA CCG       240
     Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro
20   65                  70                  75                  80

     GCA GAG CTC TGC GAG TTC TAC TCG CGC GAC CCC GAC GGG CTG CCC TGC       288
     Ala Glu Leu Cys Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys
                      85                  90                  95
25

     AAC CTG CGC AAG CCG TGC AAC CGG CCG TCG GGC CTC GAG CCG CAG CCG       336
     Asn Leu Arg Lys Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro
                  100                 105                 110

30   GGG GTC TTC GAC TGC CTG CGA GAC GCC ATG GTG CGT GAC TAC GTG CGC       384
     Gly Val Phe Asp Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg
              115                 120                 125

     CAG ACG TGG AAG CTG GAG GGC GAG GCC CTG GAG CAG GCC ATC ATC AGC       432
35   Gln Thr Trp Lys Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser
              130                 135                 140

     CAG GCC CCG CAG GTG GAG AAG CTC ATT GCT ACG ACG GCC CAC GAG CGG       480
     Gln Ala Pro Gln Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg
40   145                 150                 155                 160

     ATG CCC TGG TAC CAC AGC AGC CTG ACG CGT GAG GAG GCC GAG CGC AAA       528
     Met Pro Trp Tyr His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys
                      165                 170                 175
45

     CTT TAC TCT GGG GCG CAG ACC GAC GGC AAG TTC CTG CTG AGG CCG CGG       576
     Leu Tyr Ser Gly Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg
                  180                 185                 190

50   AAG GAG CAG GGC ACA TAC GCC CTG TCC CTC ATC TAT GGG AAG ACG GTG       624
     Lys Glu Gln Gly Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val
                  195                 200                 205

     TAC CAC TAC CTC ATC AGC CAA GAC AAG GCG GGC AAG TAC TGC ATT CCC       672
55   Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro
              210                 215                 220
```

SUBSTITUTE SHEET (RULE 26)

```
     GAG GGC ACC AAG TTT GAC ACG CTC TGG CAG CTG GTG GAG TAT CTG AAG      720
     Glu Gly Thr Lys Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys
     225             230             235             240
 5
     CTG AAG GCG GAC GGG CTC ATC TAC TGC CTG AAG GAG GCC TGC CCC AAC      768
     Leu Lys Ala Asp Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn
                     245             250             255
10   AGC AGT GCC AGC AAC GCC TCA GGG GCT GCT GCT CCC ACA CTC CCA GCC      816
     Ser Ser Ala Ser Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala
                     260             265             270

     CAC CCA TCC ACG TTG ACT CAT CCT CAG AGA CGA ATC GAC ACC CTC AAC      864
15   His Pro Ser Thr Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn
                     275             280             285

     TCA GAT GGA TAC ACC CCT GAG CCA GCA CGC ATA ACG TCC CCA GAC AAA      912
     Ser Asp Gly Tyr Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys
20       290             295             300

     CCG CGG CCG ATG CCC ATG GAC ACG AGC GTG TAT GAG AGC CCC TAC AGC      960
     Pro Arg Pro Met Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser
     305             310             315             320
25
     GAC CCA GAG GAG CTC AAG GAC AAG AAG CTC TTC CTG AAG CGC GAT AAC     1008
     Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn
                     325             330             335

30   CTC CTC ATA GCT GAC ATT GAA CTT GGC TGC GGC AAC TTT GGC TCA GTG     1056
     Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val
                     340             345             350

     CGC CAG GGC GTG TAC CGC ATG CGC AAG AAG CAG ATC GAC GTG GCC ATC     1104
35   Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile
                 355             360             365

     AAG GTG CTG AAG CAG GGC ACG GAG AAG GCA GAC ACG GAA GAG ATG ATG     1152
     Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met
40       370             375             380

     CGC GAG GCG CAG ATC ATG CAC CAG CTG GAC AAC CCC TAC ATC GTG CGG     1200
     Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg
     385             390             395             400
45
     CTC ATT GGC GTC TGC CAG GCC GAG GCC CTC ATG CTG GTC ATG GAG ATG     1248
     Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met
                     405             410             415

50   GCT GGG GGC GGG CCG CTG CAC AAG TTC CTG GTC GGC AAG AGG GAG GAG     1296
     Ala Gly Gly Gly Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu
                     420             425             430

     ATC CCT GTG AGC AAT GTG GCC GAG CTG CTG CAC CAG GTG TCC ATG GGG     1344
55   Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly
                     435             440             445
```

SUBSTITUTE SHEET (RULE 26)

```
     ATG AAG TAC CTG GAG GAG AAG AAC TTT GTG CAC CGT GAC CTG GCG GCC    1392
     Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala
         450             455             460
5
     CGC AAC GTC CTG CTG GTT AAC CGG CAC TAC GCC AAG ATC AGC GAC TTT    1440
     Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe
     465             470             475             480
10   GGC CTC TCC AAA GCA CTG GGT GCC GAC GAC AGC TAC TAC ACT GCC CGC    1488
     Gly Leu Ser Lys Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg
                 485             490             495

     TCA GCA GGG AAG TGG CCG CTC AAG TGG TAC GCA CCC GAA TGC ATC AAC    1536
15   Ser Ala Gly Lys Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn
                 500             505             510

     TTC CGC AAG TTC TCC AGC CGC AGC GAT GTC TGG AGC TAT GGG GTC ACC    1584
     Phe Arg Lys Phe Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr
20           515             520             525

     ATG TGG GAG GCC TTG TCC TAC GGC CAG AAG CCC TAC AAG AAG ATG AAA    1632
     Met Trp Glu Ala Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys
         530             535             540
25
     GGG CCG GAG GTC ATG GCC TTC ATC GAG CAG GGC AAG CGG ATG GAG TGC    1680
     Gly Pro Glu Val Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys
     545             550             555             560

30   CCA CCA GAG TGT CCA CCC GAA CTG TAC GCA CTC ATG AGT GAC TGC TGG    1728
     Pro Pro Glu Cys Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp
                 565             570             575

     ATC TAC AAG TGG GAG GAT CGC CCC GAC TTC CTG ACC GTG GAG CAG CGC    1776
35   Ile Tyr Lys Trp Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg
                 580             585             590

     ATG CGA GCC TGT TAC TAC AGC CTG GCC AGC AAG GTG GAA GGG CCC CCA    1824
     Met Arg Ala Cys Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro
             595             600             605
40
     GGC AGC ACA CAG AAG GCT GAG GCT GCC TGT GCC TGG GAT CCA CCG GTC    1872
     Gly Ser Thr Gln Lys Ala Glu Ala Ala Cys Ala Trp Asp Pro Pro Val
             610             615             620
45
     GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC    1920
     Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
     625             630             635             640

50   ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG    1968
     Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val
                 645             650             655

     TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG    2016
55   Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
                 660             665             670
```

BNSDOCID: <WO___9845704A2_I_>

```
    TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG    2064
    Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
        675             680             685
5
    ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC    2112
    Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
        690             695             700

10  ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC    2160
    Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
    705             710             715                 720

    CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC    2208
15  Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg
                    725             730             735

    GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG    2256
    Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
                740             745             750
20
    AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG    2304
    Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu
            755             760             765
25
    GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG    2352
    Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln
        770             775             780

30  AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC    2400
    Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp
    785             790             795                 800

    GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC    2448
35  Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
                    805             810             815

    GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC    2496
    Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
40                  820             825             830

    GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG    2544
    Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu
            835             840             845
45
    GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC    2592
    Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr
        850             855             860

50  AAG TAA                                                            2598
    Lys
    865


55          (2) INFORMATION FOR SEQ ID NO:111:
```

SUBSTITUTE SHEET (RULE 26)

```
         (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 865 amino acids
            (B) TYPE: amino acid
            (C) STRANDEDNESS: single
 5          (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein
         (v) FRAGMENT TYPE: internal

10          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

    Met Pro Asp Pro Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser
     1           5                  10                 15
    Arg Ala Glu Ala Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly
15              20                  25                  30
    Leu Phe Leu Leu Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu
            35                  40                  45
    Ser Leu Val His Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln
        50                  55                  60
20  Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro
    65                  70                  75                  80
    Ala Glu Leu Cys Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys
                    85                  90                  95
    Asn Leu Arg Lys Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro
25              100                 105                 110
    Gly Val Phe Asp Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg
            115                 120                 125
    Gln Thr Trp Lys Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser
        130                 135                 140
30  Gln Ala Pro Gln Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg
    145                 150                 155                 160
    Met Pro Trp Tyr His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys
                165                 170                 175
    Leu Tyr Ser Gly Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg
35              180                 185                 190
    Lys Glu Gln Gly Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val
                195                 200                 205
    Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro
        210                 215                 220
40  Glu Gly Thr Lys Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys
    225                 230                 235                 240
    Leu Lys Ala Asp Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn
                245                 250                 255
    Ser Ser Ala Ser Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala
45              260                 265                 270
    His Pro Ser Thr Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn
                275                 280                 285
    Ser Asp Gly Tyr Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys
        290                 295                 300
50  Pro Arg Pro Met Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser
    305                 310                 315                 320
    Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn
                325                 330                 335
    Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val
55              340                 345                 350
    Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile
```

203

204

```
          355                    360                    365
    Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met
          370                    375                    380
    Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg
 5  385                    390                    395               400
    Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met
                    405                    410                    415
    Ala Gly Gly Gly Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu
                    420                    425                    430
10  Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly
                    435                    440                    445
    Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala
          450                    455                    460
    Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe
15  465                    470                    475               480
    Gly Leu Ser Lys Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg
                    485                    490                    495
    Ser Ala Gly Lys Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn
                    500                    505                    510
20  Phe Arg Lys Phe Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr
                    515                    520                    525
    Met Trp Glu Ala Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys
          530                    535                    540
    Gly Pro Glu Val Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys
25  545                    550                    555               560
    Pro Pro Glu Cys Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp
                    565                    570                    575
    Ile Tyr Lys Trp Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg
                    580                    585                    590
30  Met Arg Ala Cys Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro
          595                    600                    605
    Gly Ser Thr Gln Lys Ala Glu Ala Ala Cys Ala Trp Asp Pro Pro Val
          610                    615                    620
    Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
35  625                    630                    635               640
    Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val
                    645                    650                    655
    Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
                    660                    665                    670
40  Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
          675                    680                    685
    Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
          690                    695                    700
    Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
45  705                    710                    715               720
    Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg
                    725                    730                    735
    Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
                    740                    745                    750
50  Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu
                    755                    760                    765
    Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln
          770                    775                    780
    Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp
55  785                    790                    795               800
    Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
```

SUBSTITUTE SHEET (RULE 26)

```
               805                810                815
     Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
               820                825                830
     Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu
5              835                840                845
     Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr
         850                855                860
     Lys
     865
10
                 (2)  INFORMATION FOR SEQ ID NO:112:

                 (i)  SEQUENCE CHARACTERISTICS:
                   (A)  LENGTH: 1635 base pairs
15                 (B)  TYPE: nucleic acid
                   (C)  STRANDEDNESS: single
                   (D)  TOPOLOGY: linear

                 (ii)  MOLECULE TYPE: cDNA
20               (ix)  FEATURE:

                   (A)  NAME/KEY: Coding Sequence
                   (B)  LOCATION: 1...1632
                   (D)  OTHER INFORMATION:
25
                 (xi)  SEQUENCE DESCRIPTION: SEQ ID NO:112:

     ATG GAG AAC TTC CAA AAG GTG GAA AAG ATC GGA GAG GGC ACG TAC GGA      48
     Met Glu Asn Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly
30   1               5                   10                  15

     GTT GTG TAC AAA GCC AGA AAC AAG TTG ACG GGA GAG GTG GTG GCG CTT      96
     Val Val Tyr Lys Ala Arg Asn Lys Leu Thr Gly Glu Val Val Ala Leu
                 20                  25                  30
35
     AAG AAA ATC CGC CTG GAC ACT GAG ACT GAG GGT GTG CCC AGT ACT GCC     144
     Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu Gly Val Pro Ser Thr Ala
                 35                  40                  45

40   ATC CGA GAG ATC TCT CTG CTT AAG GAG CTT AAC CAT CCT AAT ATT GTC     192
     Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Asn His Pro Asn Ile Val
                 50                  55                  60

     AAG CTG CTG GAT GTC ATT CAC ACA GAA AAT AAA CTC TAC CTG GTT TTT     240
45   Lys Leu Leu Asp Val Ile His Thr Glu Asn Lys Leu Tyr Leu Val Phe
     65                  70                  75                  80

     GAA TTT CTG CAC CAA GAT CTC AAG AAA TTC ATG GAT GCC TCT GCT CTC     288
     Glu Phe Leu His Gln Asp Leu Lys Lys Phe Met Asp Ala Ser Ala Leu
50                       85                  90                  95

     ACT GGC ATT CCT CTT CCC CTC ATC AAG AGC TAT CTG TTC CAG CTG CTC     336
     Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu
                 100                 105                 110
55
     CAG GGC CTA GCT TTC TGC CAT TCT CAT CGG GTC CTC CAC CGA GAC CTT     384
```

205

```
          Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu
              115                 120                 125

      AAA CCT CAG AAT CTG CTT ATT AAC ACA GAG GGG GCC ATC AAG CTA GCA        432
  5   Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala
          130                 135                 140

      GAC TTT GGA CTA GCC AGA GCT TTT GGA GTC CCT GTT CGT ACT TAC ACC        480
 10   Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr
          145                 150                 155                 160

      CAT GAG GTG GTG ACC CTG TGG TAC CGA GCT CCT GAA ATC CTC CTG GGC        528
      His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly
                          165                 170                 175
 15
      TCG AAA TAT TAT TCC ACA GCT GTG GAC ATC TGG AGC CTG GGC TGC ATC        576
      Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile
                  180                 185                 190

 20   TTT GCT GAG ATG GTG ACT CGC CGG GCC CTG TTC CCT GGA GAT TCT GAG        624
      Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu
              195                 200                 205

      ATT GAC CAG CTC TTC CGG ATC TTT CGG ACT CTG GGG ACC CCA GAT GAG        672
 25   Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu
          210                 215                 220

      GTG GTG TGG CCA GGA GTT ACT TCT ATG CCT GAT TAC AAG CCA AGT TTC        720
      Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe
 30   225                 230                 235                 240

      CCC AAG TGG GCC CGG CAA GAT TTT AGT AAA GTT GTA CCT CCC CTG GAT        768
      Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp
                      245                 250                 255
 35
      GAA GAT GGA CGG AGC TTG TTA TCG CAA ATG CTG CAC TAC GAC CCT AAC        816
      Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn
                  260                 265                 270

 40   AAG CGG ATT TCG GCC AAG GCA GCC CTG GCT CAC CCT TTC TTC CAG GAT        864
      Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp
              275                 280                 285

      GTG ACC AAG CCA GTA CCC CAT CTT CGA CTC TGG GAT CCA CCG GTC GCC        912
 45   Val Thr Lys Pro Val Pro His Leu Arg Leu Trp Asp Pro Pro Val Ala
              290                 295                 300

      ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC        960
      Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile
 50   305                 310                 315                 320

      CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC       1008
      Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser
                          325                 330                 335
 55
      GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC       1056
```

BNSDOCID: <WO___9845704A2_I_>

```
      Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe
              340                     345                 350

   5  ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC   1104
      Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
              355                 360                 365

      ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG   1152
  10  Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
              370                 375                 380

      AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG   1200
      Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
      385                     390                 395                 400
  15
      GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC   1248
      Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
                      405                 410                 415

  20  GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG   1296
      Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
                  420                 425                 430

      GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG   1344
  25  Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu
                  435                 440                 445

      TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG   1392
      Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys
  30      450                 455                 460

      AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC   1440
      Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly
      465                 470                 475                 480
  35
      AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC   1488
      Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
                      485                 490                 495

  40  GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC   1536
      Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
                  500                 505                 510

      CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG   1584
  45  Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu
                  515                 520                 525

      TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG T 1633
      Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
  50          530                 535                 540

      AA                                                                 1635
```

  (2) INFORMATION FOR SEQ ID NO:113:

  55
      .(i) SEQUENCE CHARACTERISTICS:

208

```
        (A)  LENGTH: 544 amino acids
        (B)  TYPE: amino acid
        (C)  STRANDEDNESS: single
        (D)  TOPOLOGY: linear
5
        (ii)  MOLECULE TYPE: protein
        (v)   FRAGMENT TYPE: internal

        (xi)  SEQUENCE DESCRIPTION: SEQ ID NO:113:
10
        Met Glu Asn Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly
        1               5                   10                  15
        Val Val Tyr Lys Ala Arg Asn Lys Leu Thr Gly Glu Val Val Ala Leu
                    20                  25                  30
15      Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu Gly Val Pro Ser Thr Ala
                    35                  40                  45
        Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Asn His Pro Asn Ile Val
                    50                  55                  60
        Lys Leu Leu Asp Val Ile His Thr Glu Asn Lys Leu Tyr Leu Val Phe
20      65                  70                  75                  80
        Glu Phe Leu His Gln Asp Leu Lys Lys Phe Met Asp Ala Ser Ala Leu
                            85                  90                  95
        Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu
                        100                 105                 110
25      Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu
                        115                 120                 125
        Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala
                    130                 135                 140
        Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr
30      145                 150                 155                 160
        His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly
                        165                 170                 175
        Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile
                        180                 185                 190
35      Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu
                        195                 200                 205
        Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu
                    210                 215                 220
        Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe
40      225                 230                 235                 240
        Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp
                    245                 250                 255
        Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn
                    260                 265                 270
45      Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp
                    275                 280                 285
        Val Thr Lys Pro Val Pro His Leu Arg Leu Trp Asp Pro Pro Val Ala
                    290                 295                 300
        Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile
50      305                 310                 315                 320
        Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser
                        325                 330                 335
        Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe
                        340                 345                 350
55      Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
                        355                 360                 365
```

208

209

```
       Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
           370                 375             380
       Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
           385             390             395                 400
  5    Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
                   405             410                 415
       Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
                   420             425                 430
       Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu
 10            435             440                 445
       Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys
           450             455                 460
       Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly
       465                 470             475                 480
 15    Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
                   485             490                 495
       Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
                   500             505                 510
       Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu
 20            515             520                 525
       Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
           530             535                 540
```

          (2) INFORMATION FOR SEQ ID NO:114:

 25
          (i) SEQUENCE CHARACTERISTICS:
             (A) LENGTH: 1635 base pairs
             (B) TYPE: nucleic acid
             (C) STRANDEDNESS: single
 30   (D) TOPOLOGY: linear

          (ii) MOLECULE TYPE: cDNA
          (ix) FEATURE:

 35   (A) NAME/KEY: Coding Sequence
             (B) LOCATION: 1...1632
             (D) OTHER INFORMATION:

          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:
 40
```
       ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG        48
       Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
        1               5               10                  15
```

```
 45    GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC        96
       Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                       20              25                  30
```

```
       GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC       144
 50    Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                   35              40                  45
```

```
       TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC       192
       Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 55        50              55                  60
```

209

210

```
       CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG      240
       Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
       65              70              75              80

  5    CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG      288
       Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                       85              90              95

       CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG      336
  10   Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                       100             105             110

       GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC      384
       Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
  15                  115             120             125

       ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC      432
       Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                       130             135             140
  20
       AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC      480
       Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
       145             150             155             160

  25   GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
       Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                           165             170             175

       GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
  30   Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                       180             185             190

       CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
       Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
  35                  195             200             205

       AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
       Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                       210             215             220
  40
       GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
       Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
       225             230             235             240

  45   GGA CTC AGA TCT CGA GCC ATG GAG AAC TTC CAA AAG GTG GAA AAG ATC      768
       Gly Leu Arg Ser Arg Ala Met Glu Asn Phe Gln Lys Val Glu Lys Ile
                           245             250             255

       GGA GAG GGC ACG TAC GGA GTT GTG TAC AAA GCC AGA AAC AAG TTG ACG      816
  50   Gly Glu Gly Thr Tyr Gly Val Val Tyr Lys Ala Arg Asn Lys Leu Thr
                       260             265             270

       GGA GAG GTG GTG GCG CTT AAG AAA ATC CGC CTG GAC ACT GAG ACT GAG      864
       Gly Glu Val Val Ala Leu Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu
  55                  275             280             285
```

210

```
     GGT GTG CCC AGT ACT GCC ATC CGA GAG ATC TCT CTG CTT AAG GAG CTT      912
     Gly Val Pro Ser Thr Ala Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu
         290                 295                 300

 5   AAC CAT CCT AAT ATT GTC AAG CTG CTG GAT GTC ATT CAC ACA GAA AAT      960
     Asn His Pro Asn Ile Val Lys Leu Leu Asp Val Ile His Thr Glu Asn
     305                 310                 315                 320

10   AAA CTC TAC CTG GTT TTT GAA TTT CTG CAC CAA GAT CTC AAG AAA TTC     1008
     Lys Leu Tyr Leu Val Phe Glu Phe Leu His Gln Asp Leu Lys Lys Phe
                         325                 330                 335

     ATG GAT GCC TCT GCT CTC ACT GGC ATT CCT CTT CCC CTC ATC AAG AGC     1056
     Met Asp Ala Ser Ala Leu Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser
15                   340                 345                 350

     TAT CTG TTC CAG CTG CTC CAG GGC CTA GCT TTC TGC CAT TCT CAT CGG     1104
     Tyr Leu Phe Gln Leu Leu Gln Gly Leu Ala Phe Cys His Ser His Arg
                 355                 360                 365
20
     GTC CTC CAC CGA GAC CTT AAA CCT CAG AAT CTG CTT ATT AAC ACA GAG     1152
     Val Leu His Arg Asp Leu Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu
             370                 375                 380

25   GGG GCC ATC AAG CTA GCA GAC TTT GGA CTA GCC AGA GCT TTT GGA GTC     1200
     Gly Ala Ile Lys Leu Ala Asp Phe Gly Leu Ala Arg Ala Phe Gly Val
     385                 390                 395                 400

     CCT GTT CGT ACT TAC ACC CAT GAG GTG GTG ACC CTG TGG TAC CGA GCT     1248
30   Pro Val Arg Thr Tyr Thr His Glu Val Val Thr Leu Trp Tyr Arg Ala
                         405                 410                 415

     CCT GAA ATC CTC CTG GGC TCG AAA TAT TAT TCC ACA GCT GTG GAC ATC     1296
     Pro Glu Ile Leu Leu Gly Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile
35                   420                 425                 430

     TGG AGC CTG GGC TGC ATC TTT GCT GAG ATG GTG ACT CGC CGG GCC CTG     1344
     Trp Ser Leu Gly Cys Ile Phe Ala Glu Met Val Thr Arg Arg Ala Leu
                 435                 440                 445
40
     TTC CCT GGA GAT TCT GAG ATT GAC CAG CTC TTC CGG ATC TTT CGG ACT     1392
     Phe Pro Gly Asp Ser Glu Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr
                 450                 455                 460

45   CTG GGG ACC CCA GAT GAG GTG GTG TGG CCA GGA GTT ACT TCT ATG CCT     1440
     Leu Gly Thr Pro Asp Glu Val Val Trp Pro Gly Val Thr Ser Met Pro
     465                 470                 475                 480

     GAT TAC AAG CCA AGT TTC CCC AAG TGG GCC CGG CAA GAT TTT AGT AAA     1488
50   Asp Tyr Lys Pro Ser Phe Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys
                         485                 490                 495

     GTT GTA CCT CCC CTG GAT GAA GAT GGA CGG AGC TTG TTA TCG CAA ATG     1536
     Val Val Pro Pro Leu Asp Glu Asp Gly Arg Ser Leu Leu Ser Gln Met
55                   500                 505                 510
```

SUBSTITUTE SHEET (RULE 26)

```
CTG CAC TAC GAC CCT AAC AAG CGG ATT TCG GCC AAG GCA GCC CTG GCT    1584
Leu His Tyr Asp Pro Asn Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala
        515                 520             525

CAC CCT TTC TTC CAG GAT GTG ACC AAG CCA GTA CCC CAT CTT CGA CTC T  1633
His Pro Phe Phe Gln Asp Val Thr Lys Pro Val Pro His Leu Arg Leu
        530                 535             540

GA                                                                 1635
```

        (2) INFORMATION FOR SEQ ID NO:115:

            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 544 amino acids
                (B) TYPE: amino acid
                (C) STRANDEDNESS: single
                (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: protein
            (v) FRAGMENT TYPE: internal

            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1               5               10              15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
        20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
        50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
        130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
        210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Met Glu Asn Phe Gln Lys Val Glu Lys Ile
                245                 250                 255
Gly Glu Gly Thr Tyr Gly Val Val Tyr Lys Ala Arg Asn Lys Leu Thr
```

```
              260                265                270
    Gly Glu Val Val Ala Leu Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu
              275                280                285
    Gly Val Pro Ser Thr Ala Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu
 5        290                295                300
    Asn His Pro Asn Ile Val Lys Leu Leu Asp Val Ile His Thr Glu Asn
    305            310                315                320
    Lys Leu Tyr Leu Val Phe Glu Phe Leu His Gln Asp Leu Lys Lys Phe
              325                330                335
10  Met Asp Ala Ser Ala Leu Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser
              340                345                350
    Tyr Leu Phe Gln Leu Leu Gln Gly Leu Ala Phe Cys His Ser His Arg
              355                360                365
    Val Leu His Arg Asp Leu Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu
15        370                375                380
    Gly Ala Ile Lys Leu Ala Asp Phe Gly Leu Ala Arg Ala Phe Gly Val
    385            390                395                400
    Pro Val Arg Thr Tyr Thr His Glu Val Val Thr Leu Trp Tyr Arg Ala
              405                410                415
20  Pro Glu Ile Leu Leu Gly Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile
              420                425                430
    Trp Ser Leu Gly Cys Ile Phe Ala Glu Met Val Thr Arg Arg Ala Leu
              435                440                445
    Phe Pro Gly Asp Ser Glu Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr
25  450            455                460
    Leu Gly Thr Pro Asp Glu Val Val Trp Pro Gly Val Thr Ser Met Pro
    465            470                475                480
    Asp Tyr Lys Pro Ser Phe Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys
              485                490                495
30  Val Val Pro Pro Leu Asp Glu Asp Gly Arg Ser Leu Leu Ser Gln Met
              500                505                510
    Leu His Tyr Asp Pro Asn Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala
              515                520                525
    His Pro Phe Phe Gln Asp Val Thr Lys Pro Val Pro His Leu Arg Leu
35  530                535                540
```

          (2) INFORMATION FOR SEQ ID NO:116:

          (i) SEQUENCE CHARACTERISTICS:
40   (A) LENGTH: 2532 base pairs
              (B) TYPE: nucleic acid
              (C) STRANDEDNESS: single
              (D) TOPOLOGY: linear

45   (ii) MOLECULE TYPE: cDNA
          (ix) FEATURE:

              (A) NAME/KEY: Coding Sequence
              (B) LOCATION: 1...2529
50   (D) OTHER INFORMATION:

          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:

```
    ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
55  Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
    1               5                   10                  15
```

SUBSTITUTE SHEET (RULE 26)

```
     GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC     96
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
              20                  25                  30
 5

     GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC    144
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                  35                  40                  45

10   TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC    192
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
              50                  55                  60

     CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG    240
15   Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80

     CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG    288
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
20                   85                  90                  95

     CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG    336
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                  100                 105                 110
25

     GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC    384
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                  115                 120                 125

30   ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC    432
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
              130                 135                 140

     AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC    480
35   Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160

     GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC    528
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
40                   165                 170                 175

     GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC    576
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                  180                 185                 190
45

     CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                  195                 200                 205

50   AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
              210                 215                 220

     GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
55   Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240
```

SUBSTITUTE SHEET (RULE 26)

215

GGA CTC AGA TCT CGA GAG ATG CTG TCC CGT GGG TGG TTT CAC CGA GAC   768
Gly Leu Arg Ser Arg Glu Met Leu Ser Arg Gly Trp Phe His Arg Asp
            245   250   255

5

CTC AGT GGG CTG GAT GCA GAG ACC CTG CTC AAG GGC CGA GGT GTC CAC   816
Leu Ser Gly Leu Asp Ala Glu Thr Leu Leu Lys Gly Arg Gly Val His
            260   265   270

10 GGT AGC TTC CTG GCT CGG CCC AGT CGC AAG AAC CAG GGT GAC TTC TCG   864
    Gly Ser Phe Leu Ala Arg Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser
                275   280   285

    CTC TCC GTC AGG GTG GGG GAT CAG GTG ACC CAT ATT CGG ATC CAG AAC   912
15 Leu Ser Val Arg Val Gly Asp Gln Val Thr His Ile Arg Ile Gln Asn
                290   295   300

    TCA GGG GAT TTC TAT GAC CTG TAT GGA GGG GAG AAG TTT GCG ACT CTG   960
    Ser Gly Asp Phe Tyr Asp Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu
20 305   310   315   320

    ACA GAG CTG GTG GAG TAC TAC ACT CAG CAG CAG GGT GTC CTG CAG GAC   1008
    Thr Glu Leu Val Glu Tyr Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp
                    325   330   335

25

    CGC GAC GGC ACC ATC ATC CAC CTC AAG TAC CCG CTG AAC TGC TCC GAT   1056
    Arg Asp Gly Thr Ile Ile His Leu Lys Tyr Pro Leu Asn Cys Ser Asp
                    340   345   350

30 CCC ACT AGT GAG AGG TGG TAC CAT GGC CAC ATG TCT GGC GGG CAG GCA   1104
    Pro Thr Ser Glu Arg Trp Tyr His Gly His Met Ser Gly Gly Gln Ala
                355   360   365

    GAG ACG CTG CTG CAG GCC AAG GGC GAG CCC TGG ACG TTT CTT GTG CGT   1152
35 Glu Thr Leu Leu Gln Ala Lys Gly Glu Pro Trp Thr Phe Leu Val Arg
                370   375   380

    GAG AGC CTC AGC CAG CCT GGA GAC TTC GTG CTT TCT GTG CTC AGT GAC   1200
    Glu Ser Leu Ser Gln Pro Gly Asp Phe Val Leu Ser Val Leu Ser Asp
40 385   390   395   400

    CAG CCC AAG GCT GGC CCA GGC TCC CCG CTC AGG GTC ACC CAC ATC AAG   1248
    Gln Pro Lys Ala Gly Pro Gly Ser Pro Leu Arg Val Thr His Ile Lys
                405   410   415

45
    GTC ATG TGC GAG GGT GGA CGC TAC ACA GTG GGT GGT TTG GAG ACC TTC   1296
    Val Met Cys Glu Gly Gly Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe
                420   425   430

50 GAC AGC CTC ACG GAC CTG GTA GAG CAT TTC AAG AAG ACG GGG ATT GAG   1344
    Asp Ser Leu Thr Asp Leu Val Glu His Phe Lys Lys Thr Gly Ile Glu
                435   440   445

    GAG GCC TCA GGC GCC TTT GTC TAC CTG CGG CAG CCG TAC TAT GCC ACG   1392
55 Glu Ala Ser Gly Ala Phe Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr
                450   455   460

                                                                          215

SUBSTITUTE SHEET (RULE 26)

216

```
     AGG GTG AAT GCG GCT GAC ATT GAG AAC CGA GTG TTG GAA CTG AAC AAG   1440
     Arg Val Asn Ala Ala Asp Ile Glu Asn Arg Val Leu Glu Leu Asn Lys
     465             470             475             480
 5

     AAG CAG GAG TCC GAG GAT ACA GCC AAG GCT GGC TTC TGG GAG GAG TTT   1488
     Lys Gln Glu Ser Glu Asp Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe
                     485             490             495

10   GAG AGT TTG CAG AAG CAG GAG GTG AAG AAC TTG CAC CAG CGT CTG GAA   1536
     Glu Ser Leu Gln Lys Gln Glu Val Lys Asn Leu His Gln Arg Leu Glu
                 500             505             510

     GGG CAG CGG CCA GAG AAC AAG GGC AAG AAC CGC TAC AAG AAC ATT CTC   1584
15   Gly Gln Arg Pro Glu Asn Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu
                 515             520             525

     CCC TTT GAC CAC AGC CGA GTG ATC CTG CAG GGA CGG GAC AGT AAC ATC   1632
     Pro Phe Asp His Ser Arg Val Ile Leu Gln Gly Arg Asp Ser Asn Ile
20   530             535             540

     CCC GGG TCC GAC TAC ATC AAT GCC AAC TAC ATC AAG AAC CAG CTG CTA   1680
     Pro Gly Ser Asp Tyr Ile Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu
     545             550             555             560
25

     GGC CCT GAT GAG AAC GCT AAG ACC TAC ATC GCC AGC CAG GGC TGT CTG   1728
     Gly Pro Asp Glu Asn Ala Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu
                     565             570             575

30   GAG GCC ACG GTC AAT GAC TTC TGG CAG ATG GCG TGG CAG GAG AAC AGC   1776
     Glu Ala Thr Val Asn Asp Phe Trp Gln Met Ala Trp Gln Glu Asn Ser
                 580             585             590

     CGT GTC ATC GTC ATG ACC ACC CGA GAG GTG GAG AAA GGC CGG AAC AAA   1824
35   Arg Val Ile Val Met Thr Thr Arg Glu Val Glu Lys Gly Arg Asn Lys
                 595             600             605

     TGC GTC CCA TAC TGG CCC GAG GTG GGC ATG CAG CGT GCT TAT GGG CCC   1872
     Cys Val Pro Tyr Trp Pro Glu Val Gly Met Gln Arg Ala Tyr Gly Pro
40   610             615             620

     TAC TCT GTG ACC AAC TGC GGG GAG CAT GAC ACA ACC GAA TAC AAA CTC   1920
     Tyr Ser Val Thr Asn Cys Gly Glu His Asp Thr Thr Glu Tyr Lys Leu
     625             630             635             640
45

     CGT ACC TTA CAG GTC TCC CCG CTG GAC AAT GGA GAC CTG ATT CGG GAG   1968
     Arg Thr Leu Gln Val Ser Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu
                 645             650             655

50   ATC TGG CAT TAC CAG TAC CTG AGC TGG CCC GAC CAT GGG GTC CCC AGT   2016
     Ile Trp His Tyr Gln Tyr Leu Ser Trp Pro Asp His Gly Val Pro Ser
                 660             665             670

     GAG CCT GGG GGT GTC CTC AGC TTC CTG GAC CAG ATC AAC CAG CGG CAG   2064
55   Glu Pro Gly Gly Val Leu Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln
                 675             680             685
```

216

SUBSTITUTE SHEET (RULE 26)

```
     GAA AGT CTG CCT CAC GCA GGG CCC ATC ATC GTG CAC TGC AGC GCC GGC        2112
     Glu Ser Leu Pro His Ala Gly Pro Ile Ile Val His Cys Ser Ala Gly
         690             695             700
5
     ATC GGC CGC ACA GGC ACC ATC ATT GTC ATC GAC ATG CTC ATG GAG AAC        2160
     Ile Gly Arg Thr Gly Thr Ile Ile Val Ile Asp Met Leu Met Glu Asn
     705             710             715             720

10   ATC TCC ACC AAG GGC CTG GAC TGT GAC ATT GAC ATC CAG AAG ACC ATC        2208
     Ile Ser Thr Lys Gly Leu Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile
                     725             730             735

     CAG ATG GTG CGG GCG CAG CGC TCG GGC ATG GTG CAG ACG GAG GCG CAG        2256
15   Gln Met Val Arg Ala Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln
                 740             745             750

     TAC AAG TTC ATC TAC GTG GCC ATC GCC CAG TTC ATT GAA ACC ACT AAG        2304
     Tyr Lys Phe Ile Tyr Val Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys
20               755             760             765

     AAG AAG CTG GAG GTC CTG CAG TCG CAG AAG GGC CAG GAG TCG GAG TAC        2352
     Lys Lys Leu Glu Val Leu Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr
         770             775             780
25
     GGG AAC ATC ACC TAT CCC CCA GCC ATG AAG AAT GCC CAT GCC AAG GCC        2400
     Gly Asn Ile Thr Tyr Pro Pro Ala Met Lys Asn Ala His Ala Lys Ala
     785             790             795             800

30   TCC CGC ACC TCG TCC AAA CAC AAG GAG GAT GTG TAT GAG AAC CTG CAC        2448
     Ser Arg Thr Ser Ser Lys His Lys Glu Asp Val Tyr Glu Asn Leu His
                     805             810             815

     ACT AAG AAC AAG AGG GAG GAG AAA GTG AAG AAG CAG CGG TCA GCA GAC        2496
35   Thr Lys Asn Lys Arg Glu Glu Lys Val Lys Lys Gln Arg Ser Ala Asp
                 820             825             830

     AAG GAG AAG AGC AAG GGT TCC CTC AAG AGG AAG TGA                        2532
     Lys Glu Lys Ser Lys Gly Ser Leu Lys Arg Lys
40           835             840
```

          (2) INFORMATION FOR SEQ ID NO:117:

45   (i) SEQUENCE CHARACTERISTICS:
                  (A) LENGTH: 843 amino acids
                  (B) TYPE: amino acid
                  (C) STRANDEDNESS: single
                  (D) TOPOLOGY: linear
50
              (ii) MOLECULE TYPE: protein
              (v) FRAGMENT TYPE: internal

              (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:
55
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu

218

```
     1                5                    10                   15
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
               20                   25                   30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 5             35                   40                   45
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
               50                   55                   60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                   70                   75                   80
10   Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                    85                   90                   95
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
               100                  105                  110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
15             115                  120                  125
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
          130                  135                  140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                  150                  155                  160
20   Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                    165                  170                  175
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
               180                  185                  190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
25             195                  200                  205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
          210                  215                  220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                  230                  235                  240
30   Gly Leu Arg Ser Arg Glu Met Leu Ser Arg Gly Trp Phe His Arg Asp
                    245                  250                  255
     Leu Ser Gly Leu Asp Ala Glu Thr Leu Leu Lys Gly Arg Gly Val His
               260                  265                  270
     Gly Ser Phe Leu Ala Arg Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser
35             275                  280                  285
     Leu Ser Val Arg Val Gly Asp Gln Val Thr His Ile Arg Ile Gln Asn
          290                  295                  300
     Ser Gly Asp Phe Tyr Asp Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu
     305                  310                  315                  320
40   Thr Glu Leu Val Glu Tyr Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp
                    325                  330                  335
     Arg Asp Gly Thr Ile Ile His Leu Lys Tyr Pro Leu Asn Cys Ser Asp
               340                  345                  350
     Pro Thr Ser Glu Arg Trp Tyr His Gly His Met Ser Gly Gly Gln Ala
45             355                  360                  365
     Glu Thr Leu Leu Gln Ala Lys Gly Glu Pro Trp Thr Phe Leu Val Arg
          370                  375                  380
     Glu Ser Leu Ser Gln Pro Gly Asp Phe Val Leu Ser Val Leu Ser Asp
     385                  390                  395                  400
50   Gln Pro Lys Ala Gly Pro Gly Ser Pro Leu Arg Val Thr His Ile Lys
                    405                  410                  415
     Val Met Cys Glu Gly Gly Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe
               420                  425                  430
     Asp Ser Leu Thr Asp Leu Val Glu His Phe Lys Lys Thr Gly Ile Glu
55             435                  440                  445
     Glu Ala Ser Gly Ala Phe Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr
```

```
                    450                    455                    460
      Arg Val Asn Ala Ala Asp Ile Glu Asn Arg Val Leu Glu Leu Asn Lys
      465                    470                    475                    480
      Lys Gln Glu Ser Glu Asp Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe
 5                        485                    490                    495
      Glu Ser Leu Gln Lys Gln Glu Val Lys Asn Leu His Gln Arg Leu Glu
                      500                    505                    510
      Gly Gln Arg Pro Glu Asn Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu
                      515                    520                    525
10    Pro Phe Asp His Ser Arg Val Ile Leu Gln Gly Arg Asp Ser Asn Ile
                      530                    535                    540
      Pro Gly Ser Asp Tyr Ile Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu
      545                    550                    555                    560
      Gly Pro Asp Glu Asn Ala Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu
15                        565                    570                    575
      Glu Ala Thr Val Asn Asp Phe Trp Gln Met Ala Trp Gln Glu Asn Ser
                      580                    585                    590
      Arg Val Ile Val Met Thr Thr Arg Glu Val Glu Lys Gly Arg Asn Lys
                      595                    600                    605
20    Cys Val Pro Tyr Trp Pro Glu Val Gly Met Gln Arg Ala Tyr Gly Pro
                      610                    615                    620
      Tyr Ser Val Thr Asn Cys Gly Glu His Asp Thr Thr Glu Tyr Lys Leu
      625                    630                    635                    640
      Arg Thr Leu Gln Val Ser Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu
25                        645                    650                    655
      Ile Trp His Tyr Gln Tyr Leu Ser Trp Pro Asp His Gly Val Pro Ser
                      660                    665                    670
      Glu Pro Gly Gly Val Leu Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln
                      675                    680                    685
30    Glu Ser Leu Pro His Ala Gly Pro Ile Ile Val His Cys Ser Ala Gly
                      690                    695                    700
      Ile Gly Arg Thr Gly Thr Ile Ile Val Ile Asp Met Leu Met Glu Asn
      705                    710                    715                    720
      Ile Ser Thr Lys Gly Leu Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile
35                        725                    730                    735
      Gln Met Val Arg Ala Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln
                      740                    745                    750
      Tyr Lys Phe Ile Tyr Val Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys
                      755                    760                    765
40    Lys Lys Leu Glu Val Leu Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr
                      770                    775                    780
      Gly Asn Ile Thr Tyr Pro Pro Ala Met Lys Asn Ala His Ala Lys Ala
      785                    790                    795                    800
      Ser Arg Thr Ser Ser Lys His Lys Glu Asp Val Tyr Glu Asn Leu His
45                        805                    810                    815
      Thr Lys Asn Lys Arg Glu Glu Lys Val Lys Lys Gln Arg Ser Ala Asp
                      820                    825                    830
      Lys Glu Lys Ser Lys Gly Ser Leu Lys Arg Lys
                      835                    840
50
```

(2) INFORMATION FOR SEQ ID NO:118:

   (i) SEQUENCE CHARACTERISTICS:
     (A) LENGTH: 2562 base pairs
55   (B) TYPE: nucleic acid
     (C) STRANDEDNESS: single

```
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA
    (ix) FEATURE:

        (A) NAME/KEY: Coding Sequence
        (B) LOCATION: 1...2559
        (D) OTHER INFORMATION:

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:
```

```
ATG CTG TCC CGT GGG TGG TTT CAC CGA GAC CTC AGT GGG CTG GAT GCA      48
Met Leu Ser Arg Gly Trp Phe His Arg Asp Leu Ser Gly Leu Asp Ala
 1               5                  10                  15

GAG ACC CTG CTC AAG GGC CGA GGT GTC CAC GGT AGC TTC CTG GCT CGG      96
Glu Thr Leu Leu Lys Gly Arg Gly Val His Gly Ser Phe Leu Ala Arg
                20                  25                  30

CCC AGT CGC AAG AAC CAG GGT GAC TTC TCG CTC TCC GTC AGG GTG GGG     144
Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser Leu Ser Val Arg Val Gly
            35                  40                  45

GAT CAG GTG ACC CAT ATT CGG ATC CAG AAC TCA GGG GAT TTC TAT GAC     192
Asp Gln Val Thr His Ile Arg Ile Gln Asn Ser Gly Asp Phe Tyr Asp
            50                  55                  60

CTG TAT GGA GGG GAG AAG TTT GCG ACT CTG ACA GAG CTG GTG GAG TAC     240
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Thr Glu Leu Val Glu Tyr
65                  70                  75                  80

TAC ACT CAG CAG CAG GGT GTC CTG CAG GAC CGC GAC GGC ACC ATC ATC     288
Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp Arg Asp Gly Thr Ile Ile
                    85                  90                  95

CAC CTC AAG TAC CCG CTG AAC TGC TCC GAT CCC ACT AGT GAG AGG TGG     336
His Leu Lys Tyr Pro Leu Asn Cys Ser Asp Pro Thr Ser Glu Arg Trp
                100                 105                 110

TAC CAT GGC CAC ATG TCT GGC GGG CAG GCA GAG ACG CTG CTG CAG GCC     384
Tyr His Gly His Met Ser Gly Gly Gln Ala Glu Thr Leu Leu Gln Ala
            115                 120                 125

AAG GGC GAG CCC TGG ACG TTT CTT GTG CGT GAG AGC CTC AGC CAG CCT     432
Lys Gly Glu Pro Trp Thr Phe Leu Val Arg Glu Ser Leu Ser Gln Pro
            130                 135                 140

GGA GAC TTC GTG CTT TCT GTG CTC AGT GAC CAG CCC AAG GCT GGC CCA     480
Gly Asp Phe Val Leu Ser Val Leu Ser Asp Gln Pro Lys Ala Gly Pro
145                 150                 155                 160

GGC TCC CCG CTC AGG GTC ACC CAC ATC AAG GTC ATG TGC GAG GGT GGA     528
Gly Ser Pro Leu Arg Val Thr His Ile Lys Val Met Cys Glu Gly Gly
                165                 170                 175

CGC TAC ACA GTG GGT GGT TTG GAG ACC TTC GAC AGC CTC ACG GAC CTG     576
Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe Asp Ser Leu Thr Asp Leu
```

221

```
       Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe Asp Ser Leu Thr Asp Leu
               180                 185                 190

       GTA GAG CAT TTC AAG AAG ACG GGG ATT GAG GAG GCC TCA GGC GCC TTT        624
 5     Val Glu His Phe Lys Lys Thr Gly Ile Glu Glu Ala Ser Gly Ala Phe
               195                 200                 205

       GTC TAC CTG CGG CAG CCG TAC TAT GCC ACG AGG GTG AAT GCG GCT GAC        672
10     Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr Arg Val Asn Ala Ala Asp
               210                 215                 220

       ATT GAG AAC CGA GTG TTG GAA CTG AAC AAG AAG CAG GAG TCC GAG GAT        720
       Ile Glu Asn Arg Val Leu Glu Leu Asn Lys Lys Gln Glu Ser Glu Asp
       225                 230                 235                 240
15
       ACA GCC AAG GCT GGC TTC TGG GAG GAG TTT GAG AGT TTG CAG AAG CAG        768
       Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe Glu Ser Leu Gln Lys Gln
                           245                 250                 255

20     GAG GTG AAG AAC TTG CAC CAG CGT CTG GAA GGG CAG CGG CCA GAG AAC        816
       Glu Val Lys Asn Leu His Gln Arg Leu Glu Gly Gln Arg Pro Glu Asn
                       260                 265                 270

       AAG GGC AAG AAC CGC TAC AAG AAC ATT CTC CCC TTT GAC CAC AGC CGA        864
25     Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Ser Arg
                       275                 280                 285

       GTG ATC CTG CAG GGA CGG GAC AGT AAC ATC CCC GGG TCC GAC TAC ATC        912
       Val Ile Leu Gln Gly Arg Asp Ser Asn Ile Pro Gly Ser Asp Tyr Ile
30             290                 295                 300

       AAT GCC AAC TAC ATC AAG AAC CAG CTG CTA GGC CCT GAT GAG AAC GCT        960
       Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu Gly Pro Asp Glu Asn Ala
       305                 310                 315                 320
35
       AAG ACC TAC ATC GCC AGC CAG GGC TGT CTG GAG GCC ACG GTC AAT GAC       1008
       Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu Glu Ala Thr Val Asn Asp
                           325                 330                 335

40     TTC TGG CAG ATG GCG TGG CAG GAG AAC AGC CGT GTC ATC GTC ATG ACC       1056
       Phe Trp Gln Met Ala Trp Gln Glu Asn Ser Arg Val Ile Val Met Thr
                           340                 345                 350

       ACC CGA GAG GTG GAG AAA GGC CGG AAC AAA TGC GTC CCA TAC TGG CCC       1104
45     Thr Arg Glu Val Glu Lys Gly Arg Asn Lys Cys Val Pro Tyr Trp Pro
                           355                 360                 365

       GAG GTG GGC ATG CAG CGT GCT TAT GGG CCC TAC TCT GTG ACC AAC TGC       1152
       Glu Val Gly Met Gln Arg Ala Tyr Gly Pro Tyr Ser Val Thr Asn Cys
50             370                 375                 380

       GGG GAG CAT GAC ACA ACC GAA TAC AAA CTC CGT ACC TTA CAG GTC TCC       1200
       Gly Glu His Asp Thr Thr Glu Tyr Lys Leu Arg Thr Leu Gln Val Ser
       385                 390                 395                 400
55
       CCG CTG GAC AAT GGA GAC CTG ATT CGG GAG ATC TGG CAT TAC CAG TAC       1248
```

221

222

```
        Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu Ile Trp His Tyr Gln Tyr
                    405             410                 415

 5      CTG AGC TGG CCC GAC CAT GGG GTC CCC AGT GAG CCT GGG GGT GTC CTC      1296
        Leu Ser Trp Pro Asp His Gly Val Pro Ser Glu Pro Gly Gly Val Leu
                    420             425                 430

        AGC TTC CTG GAC CAG ATC AAC CAG CGG CAG GAA AGT CTG CCT CAC GCA      1344
10      Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln Glu Ser Leu Pro His Ala
                    435             440                 445

        GGG CCC ATC ATC GTG CAC TGC AGC GCC GGC ATC GGC CGC ACA GGC ACC      1392
        Gly Pro Ile Ile Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr
                    450             455                 460
15
        ATC ATT GTC ATC GAC ATG CTC ATG GAG AAC ATC TCC ACC AAG GGC CTG      1440
        Ile Ile Val Ile Asp Met Leu Met Glu Asn Ile Ser Thr Lys Gly Leu
        465             470                 475                 480

20      GAC TGT GAC ATT GAC ATC CAG AAG ACC ATC CAG ATG GTG CGG GCG CAG      1488
        Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile Gln Met Val Arg Ala Gln
                        485             490                 495

        CGC TCG GGC ATG GTG CAG ACG GAG GCG CAG TAC AAG TTC ATC TAC GTG      1536
25      Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Lys Phe Ile Tyr Val
                    500             505                 510

        GCC ATC GCC CAG TTC ATT GAA ACC ACT AAG AAG AAG CTG GAG GTC CTG      1584
        Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys Lys Lys Leu Glu Val Leu
30                  515             520                 525

        CAG TCG CAG AAG GGC CAG GAG TCG GAG TAC GGG AAC ATC ACC TAT CCC      1632
        Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr Gly Asn Ile Thr Tyr Pro
                    530             535                 540
35
        CCA GCC ATG AAG AAT GCC CAT GCC AAG GCC TCC CGC ACC TCG TCC AAA      1680
        Pro Ala Met Lys Asn Ala His Ala Lys Ala Ser Arg Thr Ser Ser Lys
        545             550                 555                 560

40      CAC AAG GAG GAT GTG TAT GAG AAC CTG CAC ACT AAG AAC AAG AGG GAG      1728
        His Lys Glu Asp Val Tyr Glu Asn Leu His Thr Lys Asn Lys Arg Glu
                        565             570                 575

        GAG AAA GTG AAG AAG CAG CGG TCA GCA GAC AAG GAG AAG AGC AAG GGT      1776
45      Glu Lys Val Lys Lys Gln Arg Ser Ala Asp Lys Glu Lys Ser Lys Gly
                    580             585                 590

        TCC CTC AAG AGG AAG CGA ATT CTG CAG TCG ACG GTA CCG CGG GCC CGG      1824
        Ser Leu Lys Arg Lys Arg Ile Leu Gln Ser Thr Val Pro Arg Ala Arg
50                  595             600                 605

        GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC      1872
        Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr
                    610             615                 620
55
        GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC      1920
```
222

223

```
     Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His
     625             630             635             640

  5  AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG      1968
     Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys
                     645             650             655

 10  CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG      2016
     Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp
                 660             665             670

     CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC      2064
     Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg
                 675             680             685
 15
     TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC      2112
     Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro
                 690             695             700

 20  GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC      2160
     Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn
     705             710             715             720

     TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC      2208
 25  Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn
                     725             730             735

     CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG      2256
     Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu
 30                  740             745             750

     GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG      2304
     Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met
                 755             760             765
 35
     GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC      2352
     Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
                 770             775             780

 40  AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC      2400
     Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
     785             790             795             800

     ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG      2448
 45  Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
                     805             810             815

     AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC      2496
     Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
 50                  820             825             830

     ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG      2544
     Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
                 835             840             845
 55
     GAC GAG CTG TAC AAG TAA                                              2562
```

223

```
Asp Glu Leu Tyr Lys
    850
```

(2) INFORMATION FOR SEQ ID NO:119:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 853 amino acids
    (B) TYPE: amino acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

```
Met Leu Ser Arg Gly Trp Phe His Arg Asp Leu Ser Gly Leu Asp Ala
  1             5                  10                 15
Glu Thr Leu Leu Lys Gly Arg Gly Val His Gly Ser Phe Leu Ala Arg
          20                  25                 30
Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser Leu Ser Val Arg Val Gly
          35                  40                 45
Asp Gln Val Thr His Ile Arg Ile Gln Asn Ser Gly Asp Phe Tyr Asp
          50                  55                 60
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Thr Glu Leu Val Glu Tyr
 65                  70                 75                 80
Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp Arg Asp Gly Thr Ile Ile
                85                 90                 95
His Leu Lys Tyr Pro Leu Asn Cys Ser Asp Pro Thr Ser Glu Arg Trp
         100                 105                110
Tyr His Gly His Met Ser Gly Gly Gln Ala Glu Thr Leu Leu Gln Ala
         115                 120                125
Lys Gly Glu Pro Trp Thr Phe Leu Val Arg Glu Ser Leu Ser Gln Pro
         130                 135                140
Gly Asp Phe Val Leu Ser Val Leu Ser Asp Gln Pro Lys Ala Gly Pro
145                 150                 155                160
Gly Ser Pro Leu Arg Val Thr His Ile Lys Val Met Cys Glu Gly Gly
             165                 170                175
Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe Asp Ser Leu Thr Asp Leu
         180                 185                190
Val Glu His Phe Lys Lys Thr Gly Ile Glu Glu Ala Ser Gly Ala Phe
         195                 200                205
Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr Arg Val Asn Ala Ala Asp
         210                 215                220
Ile Glu Asn Arg Val Leu Glu Leu Asn Lys Lys Gln Glu Ser Glu Asp
225                 230                 235                240
Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe Glu Ser Leu Gln Lys Gln
             245                 250                255
Glu Val Lys Asn Leu His Gln Arg Leu Glu Gly Gln Arg Pro Glu Asn
         260                 265                270
Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Ser Arg
         275                 280                285
Val Ile Leu Gln Gly Arg Asp Ser Asn Ile Pro Gly Ser Asp Tyr Ile
         290                 295                300
Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu Gly Pro Asp Glu Asn Ala
```

```
      305                    310                    315                    320
      Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu Glu Ala Thr Val Asn Asp
                      325                    330                    335
      Phe Trp Gln Met Ala Trp Gln Glu Asn Ser Arg Val Ile Val Met Thr
  5                   340                    345                    350
      Thr Arg Glu Val Glu Lys Gly Arg Asn Lys Cys Val Pro Tyr Trp Pro
                  355                    360                    365
      Glu Val Gly Met Gln Arg Ala Tyr Gly Pro Tyr Ser Val Thr Asn Cys
                  370                    375                    380
 10   Gly Glu His Asp Thr Thr Glu Tyr Lys Leu Arg Thr Leu Gln Val Ser
      385                    390                    395                    400
      Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu Ile Trp His Tyr Gln Tyr
                      405                    410                    415
      Leu Ser Trp Pro Asp His Gly Val Pro Ser Glu Pro Gly Gly Val Leu
 15                   420                    425                    430
      Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln Glu Ser Leu Pro His Ala
                  435                    440                    445
      Gly Pro Ile Ile Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr
                  450                    455                    460
 20   Ile Ile Val Ile Asp Met Leu Met Glu Asn Ile Ser Thr Lys Gly Leu
      465                    470                    475                    480
      Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile Gln Met Val Arg Ala Gln
                      485                    490                    495
      Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Lys Phe Ile Tyr Val
 25                   500                    505                    510
      Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys Lys Lys Leu Glu Val Leu
                  515                    520                    525
      Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr Gly Asn Ile Thr Tyr Pro
                  530                    535                    540
 30   Pro Ala Met Lys Asn Ala His Ala Lys Ala Ser Arg Thr Ser Ser Lys
      545                    550                    555                    560
      His Lys Glu Asp Val Tyr Glu Asn Leu His Thr Lys Asn Lys Arg Glu
                      565                    570                    575
      Glu Lys Val Lys Lys Gln Arg Ser Ala Asp Lys Glu Lys Ser Lys Gly
 35                   580                    585                    590
      Ser Leu Lys Arg Lys Arg Ile Leu Gln Ser Thr Val Pro Arg Ala Arg
                  595                    600                    605
      Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr
                  610                    615                    620
 40   Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His
      625                    630                    635                    640
      Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys
                      645                    650                    655
      Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp
 45                   660                    665                    670
      Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg
                  675                    680                    685
      Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro
                  690                    695                    700
 50   Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn
      705                    710                    715                    720
      Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn
                      725                    730                    735
      Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu
 55                   740                    745                    750
      Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met
```

226

```
            755                760                765
     Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
            770                775                780
     Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
  5  785                790                795                800
     Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
                805                810                815
     Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
                820                825                830
 10  Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
                835                840                845
     Asp Glu Leu Tyr Lys
            850
```

15   (2) INFORMATION FOR SEQ ID NO:120:

            (i) SEQUENCE CHARACTERISTICS:
                 (A) LENGTH: 2994 base pairs
                 (B) TYPE: nucleic acid
20   (C) STRANDEDNESS: single
                 (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: cDNA
            (ix) FEATURE:
25
                 (A) NAME/KEY: Coding Sequence
                 (B) LOCATION: 1...2991
                 (D) OTHER INFORMATION:

30   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

```
     ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG    48
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                10                15
35
     GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC    96
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                    20                25                30

40   GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC   144
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                    35                40                45

     TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC   192
45   Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                    50                55                60

     CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG   240
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
50   65                70                75                80

     CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG   288
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                    85                90                95
55
     CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG   336
```

226

SUBSTITUTE SHEET (RULE 26)

227

```
        Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100             105             110

    5   GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC    384
        Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                    115             120             125

        ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC    432
        Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    10          130             135             140

        AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC    480
        Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
        145             150             155             160
    15
        GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC    528
        Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                        165             170             175

    20  GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC    576
        Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                    180             185             190

        CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
    25  Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                    195             200             205

        AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
        Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    30      210             215             220

        GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
        Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
        225             230             235             240
    35
        GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG ACC ATG GAG CGG CCC    768
        Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Glu Arg Pro
                        245             250             255

    40  CCG GGG CTG CGG CCG GGC GCG GGC GGG CCC TGG GAG ATG CGG GAG CGG    816
        Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu Met Arg Glu Arg
                    260             265             270

        CTG GGC ACC GGC GGC TTC GGG AAC GTC TGT CTG TAC CAG CAT CGG GAA    864
    45  Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr Gln His Arg Glu
                    275             280             285

        CTT GAT CTC AAA ATA GCA ATT AAG TCT TGT CGC CTA GAG CTA AGT ACC    912
        Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu Glu Leu Ser Thr
    50          290             295             300

        AAA AAC AGA GAA CGA TGG TGC CAT GAA ATC CAG ATT ATG AAG AAG TTG    960
        Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile Met Lys Lys Leu
        305             310             315             320
    55
        AAC CAT GCC AAT GTT GTA AAG GCC TGT GAT GTT CCT GAA GAA TTG AAT    1008
```

227

228

```
            Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro Glu Glu Leu Asn
                            325             330             335

      5     ATT TTG ATT CAT GAT GTG CCT CTT CTA GCA ATG GAA TAC TGT TCT GGA   1056
            Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu Tyr Cys Ser Gly
                            340             345             350

            GGA GAT CTC CGA AAG CTG CTC AAC AAA CCA GAA AAT TGT TGT GGA CTT   1104
            Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn Cys Cys Gly Leu
      10                355             360             365

            AAA GAA AGC CAG ATA CTT TCT TTA CTA AGT GAT ATA GGG TCT GGG ATT   1152
            Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile Gly Ser Gly Ile
                            370             375             380
      15
            CGA TAT TTG CAT GAA AAC AAA ATT ATA CAT CGA GAT CTA AAA CCT GAA   1200
            Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp Leu Lys Pro Glu
            385                 390             395                 400

      20    AAC ATA GTT CTT CAG GAT GTT GGT GGA AAG ATA ATA CAT AAA ATA ATT   1248
            Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile His Lys Ile Ile
                                405             410             415

            GAT CTG GGA TAT GCC AAA GAT GTT GAT CAA GGA AGT CTG TGT ACA TCT   1296
      25    Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser Leu Cys Thr Ser
                            420             425             430

            TTT GTG GGA ACA CTG CAG TAT CTG GCC CCA GAG CTC TTT GAG AAT AAG   1344
            Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu Phe Glu Asn Lys
      30                435             440             445

            CCT TAC ACA GCC ACT GTT GAT TAT TGG AGC TTT GGG ACC ATG GTA TTT   1392
            Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly Thr Met Val Phe
                            450             455             460
      35
            GAA TGT ATT GCT GGA TAT AGG CCT TTT TTG CAT CAT CTG CAG CCA TTT   1440
            Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His Leu Gln Pro Phe
            465                 470             475                 480

      40    ACC TGG CAT GAG AAG ATT AAG AAG AAG GAT CCA AAG TGT ATA TTT GCA   1488
            Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys Cys Ile Phe Ala
                                485             490             495

            TGT GAA GAG ATG TCA GGA GAA GTT CGG TTT AGT AGC CAT TTA CCT CAA   1536
      45    Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser His Leu Pro Gln
                            500             505             510

            CCA AAT AGC CTT TGT AGT TTA ATA GTA GAA CCC ATG GAA AAC TGG CTA   1584
            Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met Glu Asn Trp Leu
      50                515             520             525

            CAG TTG ATG TTG AAT TGG GAC CCT CAG CAG AGA GGA GGA CCT GTT GAC   1632
            Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly Gly Pro Val Asp
                            530             535             540
      55
            CTT ACT TTG AAG CAG CCA AGA TGT TTT GTA TTA ATG GAT CAC ATT TTG   1680
```

228

```
       Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met Asp His Ile Leu
       545             550             555             560

  5    AAT TTG AAG ATA GTA CAC ATC CTA AAT ATG ACT TCT GCA AAG ATA ATT   1728
       Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser Ala Lys Ile Ile
                       565             570             575

       TCT TTT CTG TTA CCA CCT GAT GAA AGT CTT CAT TCA CTA CAG TCT CGT   1776
       Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser Leu Gln Ser Arg
 10                580             585             590

       ATT GAG CGT GAA ACT GGA ATA AAT ACT GGT TCT CAA GAA CTT CTT TCA   1824
       Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln Glu Leu Leu Ser
                   595             600             605
 15
       GAG ACA GGA ATT TCT CTG GAT CCT CGG AAA CCA GCC TCT CAA TGT GTT   1872
       Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala Ser Gln Cys Val
                   610             615             620

 20    CTA GAT GGA GTT AGA GGC TGT GAT AGC TAT ATG GTT TAT TTG TTT GAT   1920
       Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val Tyr Leu Phe Asp
       625             630             635             640

       AAA AGT AAA ACT GTA TAT GAA GGG CCA TTT GCT TCC AGA AGT TTA TCT   1968
 25    Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser Arg Ser Leu Ser
                       645             650             655

       GAT TGT GTA AAT TAT ATT GTA CAG GAC AGC AAA ATA CAG CTT CCA ATT   2016
       Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile Gln Leu Pro Ile
 30                660             665             670

       ATA CAG CTG CGT AAA GTG TGG GCT GAA GCA GTG CAC TAT GTG TCT GGA   2064
       Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His Tyr Val Ser Gly
                   675             680             685
 35
       CTA AAA GAA GAC TAT AGC AGG CTC TTT CAG GGA CAA AGG GCA GCA ATG   2112
       Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln Arg Ala Ala Met
          690             695             700

 40    TTA AGT CTT CTT AGA TAT AAT GCT AAC TTA ACA AAA ATG AAG AAC ACT   2160
       Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys Met Lys Asn Thr
       705             710             715             720

       TTG ATC TCA GCA TCA CAA CAA CTG AAA GCT AAA TTG GAG TTT TTT CAC   2208
 45    Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu Glu Phe Phe His
                       725             730             735

       AAA AGC ATT CAG CTT GAC TTG GAG AGA TAC AGC GAG CAG ATG ACG TAT   2256
       Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu Gln Met Thr Tyr
 50                740             745             750

       GGG ATA TCT TCA GAA AAA ATG CTA AAA GCA TGG AAA GAA ATG GAA GAA   2304
       Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys Glu Met Glu Glu
                   755             760             765
 55
       AAG GCC ATC CAC TAT GCT GAG GTT GGT GTC ATT GGA TAC CTG GAG GAT   2352
```

230

```
        Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly Tyr Leu Glu Asp
        770             775             780
 5      CAG ATT ATG TCT TTG CAT GCT GAA ATC ATG GGG CTA CAG AAG AGC CCC      2400
        Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu Gln Lys Ser Pro
        785             790             795             800
        TAT GGA AGA CGT CAG GGA GAC TTG ATG GAA TCT CTG GAA CAG CGT GCC      2448
10      Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu Glu Gln Arg Ala
                        805             810             815
        ATT GAT CTA TAT AAG CAG TTA AAA CAC AGA CCT TCA GAT CAC TCC TAC      2496
        Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser Asp His Ser Tyr
                820             825             830
15
        AGT GAC AGC ACA GAG ATG GTG AAA ATC ATT GTG CAC ACT GTG CAG AGT      2544
        Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His Thr Val Gln Ser
                835             840             845
20      CAG GAC CGT GTG CTC AAG GAG CTG TTT GGT CAT TTG AGC AAG TTG TTG      2592
        Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu Ser Lys Leu Leu
                850             855             860
        GGC TGT AAG CAG AAG ATT ATT GAT CTA CTC CCT AAG GTG GAA GTG GCC      2640
25      Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys Val Glu Val Ala
        865             870             875             880
        CTC AGT AAT ATC AAA GAA GCT GAC AAT ACT GTC ATG TTC ATG CAG GGA      2688
        Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met Phe Met Gln Gly
30                      885             890             895
        AAA AGG CAG AAA GAA ATA TGG CAT CTC CTT AAA ATT GCC TGT ACA CAG      2736
        Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile Ala Cys Thr Gln
                        900             905             910
35
        AGT TCT GCC CGC TCT CTT GTA GGA TCC AGT CTA GAA GGT GCA GTA ACC      2784
        Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu Gly Ala Val Thr
                915             920             925
40      CCT CAG ACA TCA GCA TGG CTG CCC CCG ACT TCA GCA GAA CAT GAT CAT      2832
        Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala Glu His Asp His
                930             935             940
        TCT CTG TCA TGT GTG GTA ACT CCT CAA GAT GGG GAG ACT TCA GCA CAA      2880
45      Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu Thr Ser Ala Gln
        945             950             955             960
        ATG ATA GAA GAA AAT TTG AAC TGC CTT GGC CAT TTA AGC ACT ATT ATT      2928
        Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu Ser Thr Ile Ile
50                      965             970             975
        CAT GAG GCA AAT GAG GAA CAG GGC AAT AGT ATG ATG AAT CTT GAT TGG      2976
        His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met Asn Leu Asp Trp
                        980             985             990
55
        AGT TGG TTA ACA GAA TGA                                              2994
```

230

```
Ser Trp Leu Thr Glu
        995
```

```
        (2)  INFORMATION FOR SEQ ID NO:121:

        (i)  SEQUENCE CHARACTERISTICS:
             (A)  LENGTH: 997 amino acids
             (B)  TYPE: amino acid
             (C)  STRANDEDNESS: single
             (D)  TOPOLOGY: linear

        (ii)  MOLECULE TYPE: protein
        (v)  FRAGMENT TYPE: internal

        (xi)  SEQUENCE DESCRIPTION: SEQ ID NO:121:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
            35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
            50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
            115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
            130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
            195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
            210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Glu Arg Pro
                245                 250                 255
Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu Met Arg Glu Arg
                260                 265                 270
Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr Gln His Arg Glu
            275                 280                 285
Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu Glu Leu Ser Thr
            290                 295                 300
Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile Met Lys Lys Leu
```

231
```

```
     305                 310                 315                 320
     Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro Glu Glu Leu Asn
                     325                 330                 335
     Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu Tyr Cys Ser Gly
 5                   340                 345                 350
     Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn Cys Cys Gly Leu
                     355                 360                 365
     Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile Gly Ser Gly Ile
                     370                 375                 380
10   Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp Leu Lys Pro Glu
     385                 390                 395                 400
     Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile His Lys Ile Ile
                     405                 410                 415
     Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser Leu Cys Thr Ser
15                   420                 425                 430
     Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu Phe Glu Asn Lys
                     435                 440                 445
     Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly Thr Met Val Phe
                     450                 455                 460
20   Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His Leu Gln Pro Phe
     465                 470                 475                 480
     Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys Cys Ile Phe Ala
                     485                 490                 495
     Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser His Leu Pro Gln
25                   500                 505                 510
     Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met Glu Asn Trp Leu
                     515                 520                 525
     Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly Gly Pro Val Asp
                     530                 535                 540
30   Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met Asp His Ile Leu
     545                 550                 555                 560
     Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser Ala Lys Ile Ile
                     565                 570                 575
     Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser Leu Gln Ser Arg
35                   580                 585                 590
     Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln Glu Leu Leu Ser
                     595                 600                 605
     Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala Ser Gln Cys Val
                     610                 615                 620
40   Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val Tyr Leu Phe Asp
     625                 630                 635                 640
     Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser Arg Ser Leu Ser
                     645                 650                 655
     Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile Gln Leu Pro Ile
45                   660                 665                 670
     Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His Tyr Val Ser Gly
                     675                 680                 685
     Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln Arg Ala Ala Met
                     690                 695                 700
50   Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys Met Lys Asn Thr
     705                 710                 715                 720
     Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu Glu Phe Phe His
                     725                 730                 735
     Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu Gln Met Thr Tyr
55                   740                 745                 750
     Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys Glu Met Glu Glu
```

SUBSTITUTE SHEET (RULE 26)

```
                   755                   760                   765
       Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly Tyr Leu Glu Asp
           770                   775                   780
       Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu Gln Lys Ser Pro
 5     785                   790                   795                   800
       Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu Glu Gln Arg Ala
                           805                   810                   815
       Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser Asp His Ser Tyr
                   820                   825                   830
10     Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His Thr Val Gln Ser
                   835                   840                   845
       Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu Ser Lys Leu Leu
                   850                   855                   860
       Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys Val Glu Val Ala
15     865                   870                   875                   880
       Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met Phe Met Gln Gly
                           885                   890                   895
       Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile Ala Cys Thr Gln
                   900                   905                   910
20     Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu Gly Ala Val Thr
                   915                   920                   925
       Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala Glu His Asp His
                   930                   935                   940
       Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu Thr Ser Ala Gln
25     945                   950                   955                   960
       Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu Ser Thr Ile Ile
                           965                   970                   975
       His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met Asn Leu Asp Trp
                   980                   985                   990
30     Ser Trp Leu Thr Glu
               995


               (2)  INFORMATION FOR SEQ ID NO:122:

35             (i)  SEQUENCE CHARACTERISTICS:
                    (A)  LENGTH: 2991 base pairs
                    (B)  TYPE: nucleic acid
                    (C)  STRANDEDNESS: single
                    (D)  TOPOLOGY: linear

40
               (ii) MOLECULE TYPE: cDNA
               (ix) FEATURE:

                    (A)  NAME/KEY: Coding Sequence
45                  (B)  LOCATION: 1...2988
                    (D)  OTHER INFORMATION:

               (xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

50     ATG GAG CGG CCC CCG GGG CTG CGG CCG GGC GCG GGC GGG CCC TGG GAG       48
       Met Glu Arg Pro Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu
       1               5                   10                  15


       ATG CGG GAG CGG CTG GGC ACC GGC GGC TTC GGG AAC GTC TGT CTG TAC       96
55     Met Arg Glu Arg Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr
                   20                  25                  30
```

```
    CAG CAT CGG GAA CTT GAT CTC AAA ATA GCA ATT AAG TCT TGT CGC CTA       144
    Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu
            35              40              45
 5
    GAG CTA AGT ACC AAA AAC AGA GAA CGA TGG TGC CAT GAA ATC CAG ATT       192
    Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
            50              55              60
10  ATG AAG AAG TTG AAC CAT GCC AAT GTT GTA AAG GCC TGT GAT GTT CCT       240
    Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
    65              70              75              80
    GAA GAA TTG AAT ATT TTG ATT CAT GAT GTG CCT CTT CTA GCA ATG GAA       288
15  Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
                    85              90              95
    TAC TGT TCT GGA GGA GAT CTC CGA AAG CTG CTC AAC AAA CCA GAA AAT       336
    Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn
20              100             105             110
    TGT TGT GGA CTT AAA GAA AGC CAG ATA CTT TCT TTA CTA AGT GAT ATA       384
    Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile
            115             120             125
25
    GGG TCT GGG ATT CGA TAT TTG CAT GAA AAC AAA ATT ATA CAT CGA GAT       432
    Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp
            130             135             140
30  CTA AAA CCT GAA AAC ATA GTT CTT CAG GAT GTT GGT GGA AAG ATA ATA       480
    Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
    145             150             155             160
    CAT AAA ATA ATT GAT CTG GGA TAT GCC AAA GAT GTT GAT CAA GGA AGT       528
35  His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
                    165             170             175
    CTG TGT ACA TCT TTT GTG GGA ACA CTG CAG TAT CTG GCC CCA GAG CTC       576
    Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
40                  180             185             190
    TTT GAG AAT AAG CCT TAC ACA GCC ACT GTT GAT TAT TGG AGC TTT GGG       624
    Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
            195             200             205
45
    ACC ATG GTA TTT GAA TGT ATT GCT GGA TAT AGG CCT TTT TTG CAT CAT       672
    Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
            210             215             220
50  CTG CAG CCA TTT ACC TGG CAT GAG AAG ATT AAG AAG AAG GAT CCA AAG       720
    Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
    225             230             235             240
    TGT ATA TTT GCA TGT GAA GAG ATG TCA GGA GAA GTT CGG TTT AGT AGC       768
55  Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
                    245             250             255
```

234

SUBSTITUTE SHEET (RULE 26)

```
     CAT TTA CCT CAA CCA AAT AGC CTT TGT AGT TTA ATA GTA GAA CCC ATG        816
     His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
                 260                 265                 270
 5
     GAA AAC TGG CTA CAG TTG ATG TTG AAT TGG GAC CCT CAG CAG AGA GGA        864
     Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
                 275                 280                 285

10   GGA CCT GTT GAC CTT ACT TTG AAG CAG CCA AGA TGT TTT GTA TTA ATG        912
     Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
                 290                 295                 300

     GAT CAC ATT TTG AAT TTG AAG ATA GTA CAC ATC CTA AAT ATG ACT TCT        960
15   Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
     305                 310                 315                 320

     GCA AAG ATA ATT TCT TTT CTG TTA CCA CCT GAT GAA AGT CTT CAT TCA       1008
     Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
20                       325                 330                 335

     CTA CAG TCT CGT ATT GAG CGT GAA ACT GGA ATA AAT ACT GGT TCT CAA       1056
     Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
                     340                 345                 350
25
     GAA CTT CTT TCA GAG ACA GGA ATT TCT CTG GAT CCT CGG AAA CCA GCC       1104
     Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
                 355                 360                 365

30   TCT CAA TGT GTT CTA GAT GGA GTT AGA GGC TGT GAT AGC TAT ATG GTT       1152
     Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val
                 370                 375                 380

     TAT TTG TTT GAT AAA AGT AAA ACT GTA TAT GAA GGG CCA TTT GCT TCC       1200
35   Tyr Leu Phe Asp Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser
     385                 390                 395                 400

     AGA AGT TTA TCT GAT TGT GTA AAT TAT ATT GTA CAG GAC AGC AAA ATA       1248
     Arg Ser Leu Ser Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile
40                       405                 410                 415

     CAG CTT CCA ATT ATA CAG CTG CGT AAA GTG TGG GCT GAA GCA GTG CAC       1296
     Gln Leu Pro Ile Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His
                     420                 425                 430
45
     TAT GTG TCT GGA CTA AAA GAA GAC TAT AGC AGG CTC TTT CAG GGA CAA       1344
     Tyr Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln
                     435                 440                 445

50   AGG GCA GCA ATG TTA AGT CTT CTT AGA TAT AAT GCT AAC TTA ACA AAA       1392
     Arg Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys
                 450                 455                 460

     ATG AAG AAC ACT TTG ATC TCA GCA TCA CAA CAA CTG AAA GCT AAA TTG       1440
55   Met Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu
     465                 470                 475                 480
```

BNSDOCID: <WO___9845704A2_I_>

```
GAG TTT TTT CAC AAA AGC ATT CAG CTT GAC TTG GAG AGA TAC AGC GAG    1488
Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu
            485                 490                 495
```

5

```
CAG ATG ACG TAT GGG ATA TCT TCA GAA AAA ATG CTA AAA GCA TGG AAA    1536
Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys
            500                 505                 510
```

10

```
GAA ATG GAA GAA AAG GCC ATC CAC TAT GCT GAG GTT GGT GTC ATT GGA    1584
Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly
            515                 520                 525
```

```
TAC CTG GAG GAT CAG ATT ATG TCT TTG CAT GCT GAA ATC ATG GGG CTA    1632
Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu
15          530                 535                 540
```

```
CAG AAG AGC CCC TAT GGA AGA CGT CAG GGA GAC TTG ATG GAA TCT CTG    1680
Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu
20  545                 550                 555                 560
```

```
GAA CAG CGT GCC ATT GAT CTA TAT AAG CAG TTA AAA CAC AGA CCT TCA    1728
Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser
                565                 570                 575
```

25

```
GAT CAC TCC TAC AGT GAC AGC ACA GAG ATG GTG AAA ATC ATT GTG CAC    1776
Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His
            580                 585                 590
```

30

```
ACT GTG CAG AGT CAG GAC CGT GTG CTC AAG GAG CTG TTT GGT CAT TTG    1824
Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu
            595                 600                 605
```

```
AGC AAG TTG TTG GGC TGT AAG CAG AAG ATT ATT GAT CTA CTC CCT AAG    1872
Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
35          610                 615                 620
```

```
GTG GAA GTG GCC CTC AGT AAT ATC AAA GAA GCT GAC AAT ACT GTC ATG    1920
Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
40  625                 630                 635                 640
```

```
TTC ATG CAG GGA AAA AGG CAG AAA GAA ATA TGG CAT CTC CTT AAA ATT    1968
Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
            645                 650                 655
```

45

```
GCC TGT ACA CAG AGT TCT GCC CGC TCT CTT GTA GGA TCC AGT CTA GAA    2016
Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
            660                 665                 670
```

```
GGT GCA GTA ACC CCT CAG ACA TCA GCA TGG CTG CCC CCG ACT TCA GCA    2064
Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
50          675                 680                 685
```

```
GAA CAT GAT CAT TCT CTG TCA TGT GTG GTA ACT CCT CAA GAT GGG GAG    2112
Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu
55          690                 695                 700
```

```
     ACT TCA GCA CAA ATG ATA GAA GAA AAT TTG AAC TGC CTT GGC CAT TTA    2160
     Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu
     705             710             715             720
 5

     AGC ACT ATT ATT CAT GAG GCA AAT GAG GAA CAG GGC AAT AGT ATG ATG    2208
     Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met
                     725             730             735

10   AAT CTT GAT TGG AGT TGG TTA ACA GAA TGG GTA CCG CGG GCC CGG GAT    2256
     Asn Leu Asp Trp Ser Trp Leu Thr Glu Trp Val Pro Arg Ala Arg Asp
                 740             745             750

     CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG    2304
15   Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
                 755             760             765

     GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG    2352
     Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
20   770             775             780

     TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG    2400
     Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
     785             790             795             800
25

     ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC    2448
     Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
                     805             810             815

30   ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC    2496
     Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
                 820             825             830

     CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA    2544
35   Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
                 835             840             845

     GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC    2592
     Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
40   850             855             860

     AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC    2640
     Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
     865             870             875             880
45

     ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG    2688
     Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
                     885             890             895

50   CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC    2736
     His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
                 900             905             910

     GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC    2784
55   Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
                 915             920             925
```

237

SUBSTITUTE SHEET (RULE 26)

```
      ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC        2832
      Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
          930                 935                 940
  5
      CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC        2880
      Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
      945                 950                 955                 960

 10   ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG        2928
      Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
                      965                 970                 975

      GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC        2976
 15   Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
                      980                 985                 990

      GAG CTG TAC AAG TAA                                                    2991
      Glu Leu Tyr Lys
 20                   995
```

        (2) INFORMATION FOR SEQ ID NO:123:

 25   (i) SEQUENCE CHARACTERISTICS:
                 (A) LENGTH: 996 amino acids
                 (B) TYPE: amino acid
                 (C) STRANDEDNESS: single
                 (D) TOPOLOGY: linear
 30
            (ii) MOLECULE TYPE: protein
            (v) FRAGMENT TYPE: internal

            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:
 35
```
      Met Glu Arg Pro Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu
      1               5                   10                  15
      Met Arg Glu Arg Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr
                      20                  25                  30
 40   Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu
                  35                  40                  45
      Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
                  50                  55                  60
      Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
 45   65                  70                  75                  80
      Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
                      85                  90                  95
      Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn
                      100                 105                 110
 50   Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile
                      115                 120                 125
      Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp
                      130                 135                 140
      Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
 55   145                 150                 155                 160
      His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
```

BNSDOCID: <WO___9845704A2_I_>

239

```
                            165                    170                      175
        Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
                      180                    185                    190
        Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
5                     195                    200                    205
        Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
                210                    215                    220
        Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
        225                    230                    235                    240
10      Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
                            245                    250                    255
        His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
                      260                    265                    270
        Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
15                    275                    280                    285
        Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
                290                    295                    300
        Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
        305                    310                    315                    320
20      Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
                            325                    330                    335
        Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
                      340                    345                    350
        Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
25                    355                    360                    365
        Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val
                370                    375                    380
        Tyr Leu Phe Asp Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser
        385                    390                    395                    400
30      Arg Ser Leu Ser Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile
                            405                    410                    415
        Gln Leu Pro Ile Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His
                      420                    425                    430
        Tyr Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln
35                    435                    440                    445
        Arg Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys
                450                    455                    460
        Met Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu
        465                    470                    475                    480
40      Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu
                            485                    490                    495
        Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys
                      500                    505                    510
        Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly
45                    515                    520                    525
        Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu
                530                    535                    540
        Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu
        545                    550                    555                    560
50      Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser
                            565                    570                    575
        Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His
                      580                    585                    590
        Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu
55                    595                    600                    605
        Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
```

239

```
           610                    615                    620
     Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
     625                    630                    635                    640
     Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
5                        645                    650                    655
     Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
                         660                    665                    670
     Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
                         675                    680                    685
10   Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu
                         690                    695                    700
     Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu
     705                    710                    715                    720
     Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met
15                       725                    730                    735
     Asn Leu Asp Trp Ser Trp Leu Thr Glu Trp Val Pro Arg Ala Arg Asp
                         740                    745                    750
     Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
                         755                    760                    765
20   Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
                         770                    775                    780
     Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
     785                    790                    795                    800
     Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
25                       805                    810                    815
     Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
                         820                    825                    830
     Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
                         835                    840                    845
30   Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
                         850                    855                    860
     Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
     865                    870                    875                    880
     Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
35                       885                    890                    895
     His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
                         900                    905                    910
     Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
                         915                    920                    925
40   Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
                         930                    935                    940
     Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
     945                    950                    955                    960
     Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
45                       965                    970                    975
     Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
                         980                    985                    990
     Glu Leu Tyr Lys
                         995
50
          (2)  INFORMATION FOR SEQ ID NO:124:

          (i)  SEQUENCE CHARACTERISTICS:
               (A)  LENGTH: 1908 base pairs
55             (B)  TYPE: nucleic acid
               (C)  STRANDEDNESS: single
```

SUBSTITUTE SHEET (RULE 26)

241

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

5

      (A) NAME/KEY: Coding Sequence
      (B) LOCATION: 1...1905
      (D) OTHER INFORMATION:

10   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

```
    ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
    Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
    1               5                   10                  15
15
    GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
    Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                20                  25                  30

20  GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
    Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                35                  40                  45

    TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
25  Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                50                  55                  60

    CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
    Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
30  65                  70                  75                  80

    CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
    Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                        85                  90                  95
35
    CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
    Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                        100                 105                 110

40  GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
    Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                115                 120                 125

    ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
45  Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                130                 135                 140

    AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
    Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
50  145                 150                 155                 160

    GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
    Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                        165                 170                 175
55
    GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
```

241

SUBSTITUTE SHEET (RULE 26)

```
         Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                 180                 185                 190

5        CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
         Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                 195                 200                 205

         AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
         Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
10               210                 215                 220

         GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
         Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
         225                 230                 235                 240
15
         GGA CTC AGA TCT CGA GCT CAA GCT TCC ATG AGC GAG ACG GTC ATC ATG    768
         Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ser Glu Thr Val Ile Met
                         245                 250                 255

20       AGC GAG ACG GTC ATC TGT TCC AGC CGG GCC ACT GTG ATG CTT TAT GAT    816
         Ser Glu Thr Val Ile Cys Ser Ser Arg Ala Thr Val Met Leu Tyr Asp
                         260                 265                 270

         GAT GGC AAC AAG CGA TGG CTC CCT GCT GGC ACG GGT CCC CAG GCC TTC    864
25       Asp Gly Asn Lys Arg Trp Leu Pro Ala Gly Thr Gly Pro Gln Ala Phe
                 275                 280                 285

         AGC CGC GTC CAG ATC TAC CAC AAC CCC ACG GCC AAT TCC TTT CGC GTC    912
         Ser Arg Val Gln Ile Tyr His Asn Pro Thr Ala Asn Ser Phe Arg Val
30               290                 295                 300

         GTG GGC CGG AAG ATG CAG CCC GAC CAG CAG GTG GTC ATC AAC TGT GCC    960
         Val Gly Arg Lys Met Gln Pro Asp Gln Gln Val Val Ile Asn Cys Ala
         305                 310                 315                 320
35
         ATC GTC CGG GGT GTC AAG TAT AAC CAG GCC ACC CCC AAC TTC CAT CAG   1008
         Ile Val Arg Gly Val Lys Tyr Asn Gln Ala Thr Pro Asn Phe His Gln
                         325                 330                 335

40       TGG CGC GAC GCT CGC CAG GTC TGG GGC CTC AAC TTC GGC AGC AAG GAG   1056
         Trp Arg Asp Ala Arg Gln Val Trp Gly Leu Asn Phe Gly Ser Lys Glu
                         340                 345                 350

         GAT GCG GCC CAG TTT GCC GCC GGC ATG GCC AGT GCC CTA GAG GCG TTG   1104
45       Asp Ala Ala Gln Phe Ala Ala Gly Met Ala Ser Ala Leu Glu Ala Leu
                 355                 360                 365

         GAA GGA GGT GGG CCC CCT CCA CCC CCA GCA CTT CCC ACC TGG TCG GTC   1152
         Glu Gly Gly Gly Pro Pro Pro Pro Pro Ala Leu Pro Thr Trp Ser Val
50               370                 375                 380

         CCG AAC GGC CCC TCC CCG GAG GAG GTG GAG CAG CAG AAA AGG CAG CAG   1200
         Pro Asn Gly Pro Ser Pro Glu Glu Val Glu Gln Gln Lys Arg Gln Gln
         385                 390                 395                 400
55
         CCC GGC CCG TCG GAG CAC ATA GAG CGC CGG GTC TCC AAT GCA GGA GGC   1248
```

BNSDOCID: <WO___9845704A2_I_>

```
       Pro Gly Pro Ser Glu His Ile Glu Arg Arg Val Ser Asn Ala Gly Gly
                       405             410             415

  5    CCA CCT GCT CCC CCC GCT GGG GGT CCA CCC CCA CCA CCA GGA CCT CCC   1296
       Pro Pro Ala Pro Pro Ala Gly Gly Pro Pro Pro Pro Pro Gly Pro Pro
                   420             425             430

 10    CCT CCT CCA GGT CCC CCC CCA CCC CCA GGT TTG CCC CCT TCG GGG GTC   1344
       Pro Pro Pro Gly Pro Pro Pro Pro Pro Gly Leu Pro Pro Ser Gly Val
                   435             440             445

       CCA GCT GCA GCG CAC GGA GCA GGG GGA GGA CCA CCC CCT GCA CCC CCT   1392
       Pro Ala Ala Ala His Gly Ala Gly Gly Gly Pro Pro Pro Ala Pro Pro
                   450             455             460
 15
       CTC CCG GCA GCA CAG GGC CCT GGT GGT GGG GGA GCT GGG GCC CCA GGC   1440
       Leu Pro Ala Ala Gln Gly Pro Gly Gly Gly Gly Ala Gly Ala Pro Gly
       465             470             475             480

 20    CTG GCC GCA GCT ATT GCT GGA GCC AAA CTC AGG AAA GTC AGC AAG CAG   1488
       Leu Ala Ala Ala Ile Ala Gly Ala Lys Leu Arg Lys Val Ser Lys Gln
                   485             490             495

       GAG GAG GCC TCA GGG GGG CCC ACA GCC CCC AAA GCT GAG AGT GGT CGA   1536
 25    Glu Glu Ala Ser Gly Gly Pro Thr Ala Pro Lys Ala Glu Ser Gly Arg
                   500             505             510

       AGC GGA GGT GGG GGA CTC ATG GAA GAG ATG AAC GCC ATG CTG GCC CGG   1584
       Ser Gly Gly Gly Gly Leu Met Glu Glu Met Asn Ala Met Leu Ala Arg
 30            515             520             525

       AGA AGG AAA GCC ACG CAA GTT GGG GAG AAA ACC CCC AAG GAT GAA TCT   1632
       Arg Arg Lys Ala Thr Gln Val Gly Glu Lys Thr Pro Lys Asp Glu Ser
               530             535             540
 35
       GCC AAT CAG GAG GAG CCA GAG GCC AGA GTC CCG GCC CAG AGT GAA TCT   1680
       Ala Asn Gln Glu Glu Pro Glu Ala Arg Val Pro Ala Gln Ser Glu Ser
       545             550             555             560

 40    GTG CGG AGA CCC TGG GAG AAG AAC AGC ACA ACC TTG CCA AGG ATG AAG   1728
       Val Arg Arg Pro Trp Glu Lys Asn Ser Thr Thr Leu Pro Arg Met Lys
                   565             570             575

       TCG TCT TCT TCG GTG ACC ACT TCC GAG ACC CAA CCC TGC ACG CCC AGC   1776
 45    Ser Ser Ser Ser Val Thr Thr Ser Glu Thr Gln Pro Cys Thr Pro Ser
                   580             585             590

       TCC AGT GAT TAC TCG GAC CTA CAG AGG GTG AAA CAG GAG CTT CTG GAA   1824
       Ser Ser Asp Tyr Ser Asp Leu Gln Arg Val Lys Gln Glu Leu Leu Glu
 50            595             600             605

       GAG GTG AAG AAG GAA TTG CAG AAA GTG AAA GAG GAA ATC ATT GAA GCC   1872
       Glu Val Lys Lys Glu Leu Gln Lys Val Lys Glu Glu Ile Ile Glu Ala
               610             615             620
 55
       TTC GTC CAG GAG CTG AGG AAG CGG GGT TCT CCC TGA                   1908
       Phe Val Gln Glu Leu Arg Lys Arg Gly Ser Pro
```

                                                                          243

244

```
Phe Val Gln Glu Leu Arg Lys Arg Gly Ser Pro
625               630                   635
```

5   (2) INFORMATION FOR SEQ ID NO:125:

             (i) SEQUENCE CHARACTERISTICS:
                 (A) LENGTH: 635 amino acids
                 (B) TYPE: amino acid
10   (C) STRANDEDNESS: single
                 (D) TOPOLOGY: linear

             (ii) MOLECULE TYPE: protein
             (v) FRAGMENT TYPE: internal
15

             (xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:

```
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                  10                  15
20   Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                     20                  25                  30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                     35                  40                  45
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
25           50                  55                  60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                         85                  90                  95
30   Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                     100                 105                 110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                     115                 120                 125
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
35           130                 135                 140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                     165                 170                 175
40   Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                     180                 185                 190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                     195                 200                 205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
45           210                 215                 220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240
     Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ser Glu Thr Val Ile Met
                     245                 250                 255
50   Ser Glu Thr Val Ile Cys Ser Ser Arg Ala Thr Val Met Leu Tyr Asp
                     260                 265                 270
     Asp Gly Asn Lys Arg Trp Leu Pro Ala Gly Thr Gly Pro Gln Ala Phe
                     275                 280                 285
     Ser Arg Val Gln Ile Tyr His Asn Pro Thr Ala Asn Ser Phe Arg Val
55           290                 295                 300
     Val Gly Arg Lys Met Gln Pro Asp Gln Gln Val Val Ile Asn Cys Ala
```

244

SUBSTITUTE SHEET (RULE 26)

```
      305                    310                    315                    320
      Ile Val Arg Gly Val Lys Tyr Asn Gln Ala Thr Pro Asn Phe His Gln
                       325                    330                    335
      Trp Arg Asp Ala Arg Gln Val Trp Gly Leu Asn Phe Gly Ser Lys Glu
5                      340                    345                    350
      Asp Ala Ala Gln Phe Ala Ala Gly Met Ala Ser Ala Leu Glu Ala Leu
                   355                    360                    365
      Glu Gly Gly Gly Pro Pro Pro Pro Pro Ala Leu Pro Thr Trp Ser Val
                   370                    375                    380
10    Pro Asn Gly Pro Ser Pro Glu Glu Val Glu Gln Gln Lys Arg Gln Gln
      385                    390                    395                    400
      Pro Gly Pro Ser Glu His Ile Glu Arg Arg Val Ser Asn Ala Gly Gly
                           405                    410                    415
      Pro Pro Ala Pro Pro Ala Gly Gly Pro Pro Pro Pro Pro Gly Pro Pro
15                         420                    425                    430
      Pro Pro Pro Gly Pro Pro Pro Pro Pro Gly Leu Pro Pro Ser Gly Val
                   435                    440                    445
      Pro Ala Ala Ala His Gly Ala Gly Gly Gly Pro Pro Pro Ala Pro Pro
                   450                    455                    460
20    Leu Pro Ala Ala Gln Gly Pro Gly Gly Gly Gly Ala Gly Ala Pro Gly
      465                    470                    475                    480
      Leu Ala Ala Ala Ile Ala Gly Ala Lys Leu Arg Lys Val Ser Lys Gln
                           485                    490                    495
      Glu Glu Ala Ser Gly Gly Pro Thr Ala Pro Lys Ala Glu Ser Gly Arg
25                         500                    505                    510
      Ser Gly Gly Gly Gly Leu Met Glu Glu Met Asn Ala Met Leu Ala Arg
                   515                    520                    525
      Arg Arg Lys Ala Thr Gln Val Gly Glu Lys Thr Pro Lys Asp Glu Ser
                   530                    535                    540
30    Ala Asn Gln Glu Glu Pro Glu Ala Arg Val Pro Ala Gln Ser Glu Ser
      545                    550                    555                    560
      Val Arg Arg Pro Trp Glu Lys Asn Ser Thr Thr Leu Pro Arg Met Lys
                   565                    570                    575
      Ser Ser Ser Ser Val Thr Thr Ser Glu Thr Gln Pro Cys Thr Pro Ser
35                 580                    585                    590
      Ser Ser Asp Tyr Ser Asp Leu Gln Arg Val Lys Gln Glu Leu Leu Glu
                   595                    600                    605
      Glu Val Lys Lys Glu Leu Gln Lys Val Lys Glu Glu Ile Ile Glu Ala
                   610                    615                    620
40    Phe Val Gln Glu Leu Arg Lys Arg Gly Ser Pro
      625                    630                    635
```

                    (2) INFORMATION FOR SEQ ID NO:126:

45   (i) SEQUENCE CHARACTERISTICS:
                  (A) LENGTH: 1329 base pairs
                  (B) TYPE: nucleic acid
                  (C) STRANDEDNESS: single
                  (D) TOPOLOGY: linear
50
             (ii) MOLECULE TYPE: cDNA
             (ix) FEATURE:

                  (A) NAME/KEY: Coding Sequence
55   (B) LOCATION: 1...1326
                  (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

```
      ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG        48
 5    Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
       1               5                  10                  15

      GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC        96
      Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
10                 20                  25                  30

      GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC       144
      Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                   35                  40                  45
15
      TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC       192
      Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                 50                  55                  60

20    CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG       240
      Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
      65                  70                  75                  80

      CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG       288
25    Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                         85                  90                  95

      CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG       336
      Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
30                     100                 105                 110

      GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC       384
      Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                     115                 120                 125
35
      ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC       432
      Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                 130                 135                 140

40    AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC       480
      Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
      145                 150                 155                 160

      GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC       528
45    Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                         165                 170                 175

      GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC       576
      Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
50                     180                 185                 190

      CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG       624
      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                     195                 200                 205
55
      AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC       672
```

246

SUBSTITUTE SHEET (RULE 26)

```
        Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
            210                 215                 220

     GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC        ·720
 5   Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240

     GGA CTC AGA TCT CGA GCT CAA GCT TCA ATG GCT GCC ATC CGG AAG AAA         768
10   Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ala Ala Ile Arg Lys Lys
                     245                 250                 255

     CTG GTG ATT GTT GGT GAT GGA GCC TGT GGA AAG ACA TGC TTG CTC ATA         816
     Leu Val Ile Val Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Ile
                     260                 265                 270
15
     GTC TTC AGC AAG GAC CAG TTC CCA GAG GTG TAT GTG CCC ACA GTG TTT         864
     Val Phe Ser Lys Asp Gln Phe Pro Glu Val Tyr Val Pro Thr Val Phe
                     275                 280                 285

20   GAG AAC TAT GTG GCA GAT ATC GAG GTG GAT GGA AAG CAG GTA GAG TTG         912
     Glu Asn Tyr Val Ala Asp Ile Glu Val Asp Gly Lys Gln Val Glu Leu
                 290                 295                 300

     GCT TTG TGG GAC ACA GCT GGG CAG GAA GAT TAT GAT CGC CTG AGG CCC         960
25   Ala Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro
     305                 310                 315                 320

     CTC TCC TAC CCA GAT ACC GAT GTT ATA CTG ATG TGT TTT TCC ATC GAC        1008
     Leu Ser Tyr Pro Asp Thr Asp Val Ile Leu Met Cys Phe Ser Ile Asp
30                   325                 330                 335

     AGC CCT GAT AGT TTA GAA AAC ATC CCA GAA AAG TGG ACC CCA GAA GTC        1056
     Ser Pro Asp Ser Leu Glu Asn Ile Pro Glu Lys Trp Thr Pro Glu Val
                     340                 345                 350
35
     AAG CAT TTC TGT CCC AAC GTG CCC ATC ATC CTG GTT GGG AAT AAG AAG        1104
     Lys His Phe Cys Pro Asn Val Pro Ile Ile Leu Val Gly Asn Lys Lys
                     355                 360                 365

40   GAT CTT CGG AAT GAT GAG CAC ACA AGG CGG GAG CTA GCC AAG ATG AAG        1152
     Asp Leu Arg Asn Asp Glu His Thr Arg Arg Glu Leu Ala Lys Met Lys
                 370                 375                 380

     CAG GAG CCG GTG AAA CCT GAA GAA GGC AGA GAT ATG GCA AAC AGG ATT        1200
45   Gln Glu Pro Val Lys Pro Glu Glu Gly Arg Asp Met Ala Asn Arg Ile
     385                 390                 395                 400

     GGC GCT TTT GGG TAC ATG GAG TGT TCA GCA AAG ACC AAA GAT GGA GTG        1248
     Gly Ala Phe Gly Tyr Met Glu Cys Ser Ala Lys Thr Lys Asp Gly Val
50                   405                 410                 415

     AGA GAG GTT TTT GAA ATG GCT ACG AGA GCT GCT CTG CAA GCT AGA CGT        1296
     Arg Glu Val Phe Glu Met Ala Thr Arg Ala Ala Leu Gln Ala Arg Arg
                     420                 425                 430
55
        GGG AAG AAA AAA TCT GGT TGC CTT GTC TTG TGA                         1329
```

248

```
Gly Lys Lys Lys Ser Gly Cys Leu Val Leu
        435                 440
```

5   (2) INFORMATION FOR SEQ ID NO:127:

             (i) SEQUENCE CHARACTERISTICS:
                  (A) LENGTH: 442 amino acids
                  (B) TYPE: amino acid
10   (C) STRANDEDNESS: single
                  (D) TOPOLOGY: linear

             (ii) MOLECULE TYPE: protein
             (v) FRAGMENT TYPE: internal
15

             (xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

```
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
     1               5                   10                  15
20   Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                 20                  25                  30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                 35                  40                  45
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
25            50                  55                  60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                     85                  90                  95
30   Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                     100                 105                 110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                 115                 120                 125
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
35            130                 135                 140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                     165                 170                 175
40   Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                     180                 185                 190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                 195                 200                 205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
45            210                 215                 220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240
     Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ala Ala Ile Arg Lys Lys
                     245                 250                 255
50   Leu Val Ile Val Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Ile
                     260                 265                 270
     Val Phe Ser Lys Asp Gln Phe Pro Glu Val Tyr Val Pro Thr Val Phe
                 275                 280                 285
     Glu Asn Tyr Val Ala Asp Ile Glu Val Asp Gly Lys Gln Val Glu Leu
55            290                 295                 300
     Ala Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro
```

```
                    305                       310                       315                       320
         Leu Ser Tyr Pro Asp Thr Asp Val Ile Leu Met Cys Phe Ser Ile Asp
                             325                       330                       335
         Ser Pro Asp Ser Leu Glu Asn Ile Pro Glu Lys Trp Thr Pro Glu Val
5                            340                       345                       350
         Lys His Phe Cys Pro Asn Val Pro Ile Ile Leu Val Gly Asn Lys Lys
                     355                       360                       365
         Asp Leu Arg Asn Asp Glu His Thr Arg Arg Glu Leu Ala Lys Met Lys
                     370                       375                       380
10       Gln Glu Pro Val Lys Pro Glu Glu Gly Arg Asp Met Ala Asn Arg Ile
         385                       390                       395                       400
         Gly Ala Phe Gly Tyr Met Glu Cys Ser Ala Lys Thr Lys Asp Gly Val
                             405                       410                       415
         Arg Glu Val Phe Glu Met Ala Thr Arg Ala Ala Leu Gln Ala Arg Arg
15                           420                       425                       430
         Gly Lys Lys Lys Ser Gly Cys Leu Val Leu
                     435                       440
```

                    (2) INFORMATION FOR SEQ ID NO:128:
20
                    (i) SEQUENCE CHARACTERISTICS:
                         (A) LENGTH: 1140 base pairs
                         (B) TYPE: nucleic acid
                         (C) STRANDEDNESS: single
25   (D) TOPOLOGY: linear

                    (ii) MOLECULE TYPE: cDNA
                    (ix) FEATURE:

30   (A) NAME/KEY: Coding Sequence
                         (B) LOCATION: 1...1137
                         (D) OTHER INFORMATION:

                    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:
35
```
         ATG GAC CAT TAT GAT TCT CAG CAA ACC AAC GAT TAC ATG CAG CCA GAA          48
         Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu
         1                     5                       10                      15

40       GAG GAC TGG GAC CGG GAC CTG CTC CTG GAC CCG GCC TGG GAG AAG CAG          96
         Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln
                             20                      25                      30

         CAG AGA AAG ACA TTC ACG GCA TGG TGT AAC TCC CAC CTC CGG AAG GCG         144
45       Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala
                     35                      40                      45

         GGG ACA CAG ATC GAG AAC ATC GAA GAG GAC TTC CGG GAT GGC CTG AAG         192
         Gly Thr Gln Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys
50           50                      55                      60

         CTC ATG CTG CTG CTG GAG GTC ATC TCA GGT GAA CGC TTG GCC AAG CCA         240
         Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu Ala Lys Pro
         65                      70                      75                      80
55
         GAG CGA GGC AAG ATG AGA GTG CAC AAG ATC TCC AAC GTC AAC AAG GCC         288
```

250

```
           Glu Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val Asn Lys Ala
                           85              90              95

     5     CTG GAT TTC ATA GCC AGC AAA GGC GTC AAA CTG GTG TCC ATC GGA GCC      336
           Leu Asp Phe Ile Ala Ser Lys Gly Val Lys Leu Val Ser Ile Gly Ala
                       100             105             110

           GAA GAA ATC GTG GAT GGG AAT GTG AAG ATG ACC CTG GGC ATG ATC TGG      384
           Glu Glu Ile Val Asp Gly Asn Val Lys Met Thr Leu Gly Met Ile Trp
     10                115             120             125

           ACC ATC ATC CTG CGC AGG GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG      432
           Thr Ile Ile Leu Arg Arg Asp Pro Pro Val Ala Thr Met Val Ser Lys
                   130             135             140
     15
           GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC      480
           Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp
           145             150             155             160

     20    GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC      528
           Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly
                           165             170             175

           GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC      576
     25    Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly
                       180             185             190

           AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC      624
           Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly
     30            195             200             205

           GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC      672
           Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp Phe
                   210             215             220
     35
           TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC      720
           Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe
           225             230             235             240

     40    TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG      768
           Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu
                           245             250             255

           GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG      816
     45    Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys
                       260             265             270

           GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC      864
           Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser
     50            275             280             285

           CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG      912
           His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val
                   290             295             300
     55
           AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC      960
```

250

```
            Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala
            305                 310             315                 320

       5    GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG    1008
            Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu
                            325             330             335

            CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC    1056
      10    Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro
                        340             345             350

            AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC    1104
            Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala
                        355             360             365
      15
            GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA                    1140
            Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
                        370             375

      20
                    (2)  INFORMATION FOR SEQ ID NO:129:

                    (i)  SEQUENCE CHARACTERISTICS:
                         (A) LENGTH: 379 amino acids
      25                 (B) TYPE: amino acid
                         (C) STRANDEDNESS: single
                         (D) TOPOLOGY: linear

                    (ii) MOLECULE TYPE: protein
      30        (v)  FRAGMENT TYPE: internal

                    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

            Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu
      35    1               5               10              15
            Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln
                        20              25              30
            Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala
                        35              40              45
      40    Gly Thr Gln Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys
                    50              55              60
            Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu Ala Lys Pro
            65              70              75              80
            Glu Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val Asn Lys Ala
      45    85              90              95
            Leu Asp Phe Ile Ala Ser Lys Gly Val Lys Leu Val Ser Ile Gly Ala
                        100             105             110
            Glu Glu Ile Val Asp Gly Asn Val Lys Met Thr Leu Gly Met Ile Trp
                        115             120             125
      50    Thr Ile Ile Leu Arg Arg Asp Pro Pro Val Ala Thr Met Val Ser Lys
                    130             135             140
            Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp
            145             150             155             160
            Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly
      55                    165             170             175
            Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly
```

SUBSTITUTE SHEET (RULE 26)

252

```
                180                    185                    190
      Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly
                195                    200                    205
      Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp Phe
  5         210                    215                    220
      Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe
      225                    230                    235                    240
      Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu
                        245                    250                    255
 10   Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys
                        260                    265                    270
      Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser
                        275                    280                    285
      His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val
 15             290                    295                    300
      Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala
      305                    310                    315                    320
      Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu
                        325                    330                    335
 20   Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro
                        340                    345                    350
      Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala
                355                    360                    365
      Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 25             370                    375
```

             (2) INFORMATION FOR SEQ ID NO:130:

             (i) SEQUENCE CHARACTERISTICS:
 30   (A) LENGTH: 3516 base pairs
                 (B) TYPE: nucleic acid
                 (C) STRANDEDNESS: single
                 (D) TOPOLOGY: linear

 35   (ii) MOLECULE TYPE: cDNA
             (ix) FEATURE:

                 (A) NAME/KEY: Coding Sequence
                 (B) LOCATION: 1...3513
 40   (D) OTHER INFORMATION:

             (xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

```
      ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
 45   Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                   10                  15


      GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
      Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
 50             20                  25                  30


      GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
      Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                35                  40                  45
 55
      TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
```

252

253

```
      Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
      50                  55                  60

 5    CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG    240
      Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
      65                  70                  75                  80

      CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG    288
      Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
10                            85                  90                  95

      CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG    336
      Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                              100                 105                 110
15
      GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC    384
      Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                      115                 120                 125

20    ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC    432
      Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
              130                 135                 140

      AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC    480
25    Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
      145                 150                 155                 160

      GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC    528
      Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
30                            165                 170                 175

      GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC    576
      Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                      180                 185                 190
35
      CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                      195                 200                 205

40    AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
      Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
      210                 215                 220

      GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
45    Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
      225                 230                 235                 240

      GGA CTC AGA TCT CGA GCC ATG AAC GCC CCC GAG CGG CAG CCC CAA CCC    768
      Gly Leu Arg Ser Arg Ala Met Asn Ala Pro Glu Arg Gln Pro Gln Pro
50                            245                 250                 255

      GAC GGC GGG GAC GCC CCA GGC CAC GAG CCT GGG GGC AGC CCC CAA GAC    816
      Asp Gly Gly Asp Ala Pro Gly His Glu Pro Gly Gly Ser Pro Gln Asp
                              260                 265                 270
55
      GAG CTT GAC TTC TCC ATC CTC TTC GAC TAT GAG TAT TTG AAT CCG AAC    864
```

253

254

```
        Glu Leu Asp Phe Ser Ile Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn
            275                 280             285

    5   GAA GAA GAG CCG AAT GCA CAT AAG GTC GCC AGC CCA CCC TCC GGA CCC      912
        Glu Glu Glu Pro Asn Ala His Lys Val Ala Ser Pro Pro Ser Gly Pro
            290             295             300

   10   GCA TAC CCC GAT GAT GTA ATG GAC TAT GGC CTC AAG CCA TAC AGC CCC      960
        Ala Tyr Pro Asp Asp Val Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro
        305             310             315             320

        CTT GCT AGT CTC TCT GGC GAG CCC CCC GGC CGA TTC GGA GAG CCG GAT     1008
        Leu Ala Ser Leu Ser Gly Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp
                    325             330             335
   15
        AGG GTA GGG CCG CAG AAG TTT CTG AGC GCG GCC AAG CCA GCA GGG GCC     1056
        Arg Val Gly Pro Gln Lys Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala
                    340             345             350

   20   TCG GGC CTG AGC CCT CGG ATC GAG ATC ACT CCG TCC CAC GAA CTG ATC     1104
        Ser Gly Leu Ser Pro Arg Ile Glu Ile Thr Pro Ser His Glu Leu Ile
                    355             360             365

        CAG GCA GTG GGG CCC CTC CGC ATG AGA GAC GCG GGC CTC CTG GTG GAG     1152
   25   Gln Ala Val Gly Pro Leu Arg Met Arg Asp Ala Gly Leu Leu Val Glu
                370             375             380

        CAG CCT CCC CTG GCC GGG GTG GCC GCC AGC CCG AGG TTC ACC CTG CCC     1200
        Gln Pro Pro Leu Ala Gly Val Ala Ala Ser Pro Arg Phe Thr Leu Pro
   30   385             390             395             400

        GTG CCC GGC TTC GAG GGC TAC CGC GAG CCG CTT TGC TTG AGC CCC GCT     1248
        Val Pro Gly Phe Glu Gly Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala
                    405             410             415
   35
        AGC AGC GGC TCC TCT GCC AGC TTC ATT TCT GAC ACC TTC TCC CCC TAC     1296
        Ser Ser Gly Ser Ser Ala Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr
                    420             425             430

   40   ACC TCG CCC TGC GTC TCG CCC AAT AAC GGC GGG CCC GAC GAC CTG TGT     1344
        Thr Ser Pro Cys Val Ser Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys
                    435             440             445

        CCG CAG TTT CAA AAC ATC CCT GCT CAT TAT TCC CCC AGA ACC TCG CCA     1392
   45   Pro Gln Phe Gln Asn Ile Pro Ala His Tyr Ser Pro Arg Thr Ser Pro
            450             455             460

        ATA ATG TCA CCT CGA ACC AGC CTC GCC GAG GAC AGC TGC CTG GGC CGC     1440
        Ile Met Ser Pro Arg Thr Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg
   50   465             470             475             480

        CAC TCG CCC GTG CCC CGT CCG GCC TCC CGC TCC TCA TCG CCT GGT GCC     1488
        His Ser Pro Val Pro Arg Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala
                    485             490             495
   55
        AAG CGG AGG CAT TCG TGC GCC GAG GCC TTG GTT GCC CTG CCG CCC GGA     1536
```

                                                                           254

BNSDOCID: <WO___9845704A2_I_>

255

```
        Lys Arg Arg His Ser Cys Ala Glu Ala Leu Val Ala Leu Pro Pro Gly
                    500             505             510

  5     GCC TCA CCC CAG CGC TCC CGG AGC CCC TCG CCG CAG CCC TCA TCT CAC    1584
        Ala Ser Pro Gln Arg Ser Arg Ser Pro Ser Pro Gln Pro Ser Ser His
                515             520             525

        GTG GCA CCC CAG GAC CAC GGC TCC CCG GCT GGG TAC CCC CCT GTG GCT    1632
        Val Ala Pro Gln Asp His Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala
 10         530             535             540

        GGC TCT GCC GTG ATC ATG GAT GCC CTG AAC AGC CTC GCC ACG GAC TCG    1680
        Gly Ser Ala Val Ile Met Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser
        545             550             555             560
 15
        CCT TGT GGG ATC CCC CCC AAG ATG TGG AAG ACC AGC CCT GAC CCC TCG    1728
        Pro Cys Gly Ile Pro Pro Lys Met Trp Lys Thr Ser Pro Asp Pro Ser
                        565             570             575

 20     CCG GTG TCT GCC GCC CCA TCC AAG GCC GGC CTG CCT CGC CAC ATC TAC    1776
        Pro Val Ser Ala Ala Pro Ser Lys Ala Gly Leu Pro Arg His Ile Tyr
                    580             585             590

        CCG GCC GTG GAG TTC CTG GGG CCC TGC GAG CAG GGC GAG AGG AGA AAC    1824
 25     Pro Ala Val Glu Phe Leu Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn
                595             600             605

        TCG GCT CCA GAA TCC ATC CTG CTG GTT CCG CCC ACT TGG CCC AAG CCG    1872
        Ser Ala Pro Glu Ser Ile Leu Leu Val Pro Pro Thr Trp Pro Lys Pro
 30         610             615             620

        CTG GTG CCT GCC ATT CCC ATC TGC AGC ATC CCA GTG ACT GCA TCC CTC    1920
        Leu Val Pro Ala Ile Pro Ile Cys Ser Ile Pro Val Thr Ala Ser Leu
        625             630             635             640
 35
        CCT CCA CTT GAG TGG CCG CTG TCC AGT CAG TCA GGC TCT TAC GAG CTG    1968
        Pro Pro Leu Glu Trp Pro Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu
                        645             650             655

 40     CGG ATC GAG GTG CAG CCC AAG CCA CAT CAC CGG GCC CAC TAT GAG ACA    2016
        Arg Ile Glu Val Gln Pro Lys Pro His His Arg Ala His Tyr Glu Thr
                    660             665             670

        GAA GGC AGC CGA GGG GCT GTC AAA GCT CCA ACT GGA GGC CAC CCT GTG    2064
 45     Glu Gly Ser Arg Gly Ala Val Lys Ala Pro Thr Gly Gly His Pro Val
                675             680             685

        GTT CAG CTC CAT GGC TAC ATG GAA AAC AAG CCT CTG GGA CTT CAG ATC    2112
        Val Gln Leu His Gly Tyr Met Glu Asn Lys Pro Leu Gly Leu Gln Ile
 50         690             695             700

        TTC ATT GGG ACA GCT GAT GAG CGG ATC CTT AAG CCG CAC GCC TTC TAC    2160
        Phe Ile Gly Thr Ala Asp Glu Arg Ile Leu Lys Pro His Ala Phe Tyr
        705             710             715             720
 55
        CAG GTG CAC CGA ATC ACG GGG AAA ACT GTC ACC ACC ACC AGC TAT GAG    2208
```

255

BNSDOCID: <WO___9845704A2_I_>

256

```
            Gln Val His Arg Ile Thr Gly Lys Thr Val Thr Thr Thr Ser Tyr Glu
                        725                 730                 735

  5        AAG ATA GTG GGC AAC ACC AAA GTC CTG GAG ATC CCC TTG GAG CCC AAA    2256
            Lys Ile Val Gly Asn Thr Lys Val Leu Glu Ile Pro Leu Glu Pro Lys
                        740                 745                 750

            AAC AAC ATG AGG GCA ACC ATC GAC TGT GCG GGG ATC TTG AAG CTT AGA    2304
            Asn Asn Met Arg Ala Thr Ile Asp Cys Ala Gly Ile Leu Lys Leu Arg
 10                     755                 760                 765

            AAC GCC GAC ATT GAG CTG CGG AAA GGC GAG ACG GAC ATT GGA AGA AAG    2352
            Asn Ala Asp Ile Glu Leu Arg Lys Gly Glu Thr Asp Ile Gly Arg Lys
                        770                 775                 780
 15
            AAC ACG CGG GTG AGA CTG GTT TTC CGA GTT CAC ATC CCA GAG TCC AGT    2400
            Asn Thr Arg Val Arg Leu Val Phe Arg Val His Ile Pro Glu Ser Ser
            785                 790                 795                 800

 20        GGC AGA ATC GTC TCT TTA CAG ACT GCA TCT AAC CCC ATC GAG TGC TCC    2448
            Gly Arg Ile Val Ser Leu Gln Thr Ala Ser Asn Pro Ile Glu Cys Ser
                            805                 810                 815

            CAG CGA TCT GCT CAC GAG CTG CCC ATG GTT GAA AGA CAA GAC ACA GAC    2496
 25        Gln Arg Ser Ala His Glu Leu Pro Met Val Glu Arg Gln Asp Thr Asp
                        820                 825                 830

            AGC TGC CTG GTC TAT GGC GGC CAG CAA ATG ATC CTC ACG GGG CAG AAC    2544
            Ser Cys Leu Val Tyr Gly Gly Gln Gln Met Ile Leu Thr Gly Gln Asn
 30                     835                 840                 845

            TTT ACA TCC GAG TCC AAA GTT GTG TTT ACT GAG AAG ACC ACA GAT GGA    2592
            Phe Thr Ser Glu Ser Lys Val Val Phe Thr Glu Lys Thr Thr Asp Gly
                        850                 855                 860
 35
            CAG CAA ATT TGG GAG ATG GAA GCC ACG GTG GAT AAG GAC AAG AGC CAG    2640
            Gln Gln Ile Trp Glu Met Glu Ala Thr Val Asp Lys Asp Lys Ser Gln
            865                 870                 875                 880

 40        CCC AAC ATG CTT TTT GTT GAG ATC CCT GAA TAT CGG AAC AAG CAT ATC    2688
            Pro Asn Met Leu Phe Val Glu Ile Pro Glu Tyr Arg Asn Lys His Ile
                            885                 890                 895

            CGC ACA CCT GTA AAA GTG AAC TTC TAC GTC ATC AAT GGG AAG AGA AAA    2736
 45        Arg Thr Pro Val Lys Val Asn Phe Tyr Val Ile Asn Gly Lys Arg Lys
                        900                 905                 910

            CGA AGT CAG CCT CAG CAC TTT ACC TAC CAC CCA GTC CCA GCC ATC AAG    2784
            Arg Ser Gln Pro Gln His Phe Thr Tyr His Pro Val Pro Ala Ile Lys
 50                     915                 920                 925

            ACG GAG CCC ACG GAT GAA TAT GAC CCC ACT CTG ATC TGC AGC CCC ACC    2832
            Thr Glu Pro Thr Asp Glu Tyr Asp Pro Thr Leu Ile Cys Ser Pro Thr
                        930                 935                 940
 55
            CAT GGA GGC CTG GGG AGC CAG CCT TAC TAC CCC CAG CAC CCG ATG GTG    2880
```

256

```
        His Gly Gly Leu Gly Ser Gln Pro Tyr Tyr Pro Gln His Pro Met Val
        945             950             955             960


5       GCC GAG TCC CCC TCC TGC CTC GTG GCC ACC ATG GCT CCC TGC CAG CAG    2928
        Ala Glu Ser Pro Ser Cys Leu Val Ala Thr Met Ala Pro Cys Gln Gln
                        965             970             975


        TTC CGC ACG GGG CTC TCA TCC CCT GAC GCC CGC TAC CAG CAA CAG AAC    2976
        Phe Arg Thr Gly Leu Ser Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn
10                      980             985             990


        CCA GCG GCC GTA CTC TAC CAG CGG AGC AAG AGC CTG AGC CCC AGC CTG    3024
        Pro Ala Ala Val Leu Tyr Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu
                995             1000            1005
15

        CTG GGC TAT CAG CAG CCG GCC CTC ATG GCC GCC CCG CTG TCC CTT GCG    3072
        Leu Gly Tyr Gln Gln Pro Ala Leu Met Ala Ala Pro Leu Ser Leu Ala
            1010            1015            1020


20      GAC GCT CAC CGC TCT GTG CTG GTG CAC GCC GGC TCC CAG GGC CAG AGC    3120
        Asp Ala His Arg Ser Val Leu Val His Ala Gly Ser Gln Gly Gln Ser
        1025            1030            1035            1040


        TCA GCC CTG CTC CAC CCC TCT CCG ACC AAC CAG CAG GCC TCG CCT GTG    3168
25      Ser Ala Leu Leu His Pro Ser Pro Thr Asn Gln Gln Ala Ser Pro Val
                        1045            1050            1055


        ATC CAC TAC TCA CCC ACC AAC CAG CAG CTG CGC TGC GGA AGC CAC CAG    3216
        Ile His Tyr Ser Pro Thr Asn Gln Gln Leu Arg Cys Gly Ser His Gln
30                      1060            1065            1070


        GAG TTC CAG CAC ATC ATG TAC TGC GAG AAT TTC GCA CCA GGC ACC ACC    3264
        Glu Phe Gln His Ile Met Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr
                    1075            1080            1085
35

        AGA CCT GGC CCG CCC CCG GTC AGT CAA GGT CAG AGG CTG AGC CCG GGT    3312
        Arg Pro Gly Pro Pro Pro Val Ser Gln Gly Gln Arg Leu Ser Pro Gly
            1090            1095            1100


40      TCC TAC CCC ACA GTC ATT CAG CAG CAG AAT GCC ACG AGC CAA AGA GCC    3360
        Ser Tyr Pro Thr Val Ile Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala
        1105            1110            1115            1120


        GCC AAA AAC GGA CCC CCG GTC AGT GAC CAA AAG GAA GTA TTA CCT GCG    3408
45      Ala Lys Asn Gly Pro Pro Val Ser Asp Gln Lys Glu Val Leu Pro Ala
                        1125            1130            1135


        GGG GTG ACC ATT AAA CAG GAG CAG AAC TTG GAC CAG ACC TAC TTG GAT    3456
        Gly Val Thr Ile Lys Gln Glu Gln Asn Leu Asp Gln Thr Tyr Leu Asp
50                  1140            1145            1150


        GAT GTT AAT GAA ATT ATC AGG AAG GAG TTT TCA GGA CCT CCT GCC AGA    3504
        Asp Val Asn Glu Ile Ile Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg
                    1155            1160            1165
55
        AAT CAG ACG TAA                                                    3516
```

SUBSTITUTE SHEET (RULE 26)

Asn Gln Thr
    1170

        Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
        1   5   10   15
20   Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                        20   25   30
        Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                        35   40   45
        Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
25   50   55   60
        Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
        65   70   75   80
        Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                            85   90   95
30   Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                        100   105   110
        Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                        115   120   125
        Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
35   130   135   140
        Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
        145   150   155   160
        Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                        165   170   175
        Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
40   180   185   190
        Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                        195   200   205
        Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
45   210   215   220
        Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
        225   230   235   240
        Gly Leu Arg Ser Arg Ala Met Asn Ala Pro Glu Arg Gln Pro Gln Pro
                        245   250   255
        Asp Gly Gly Asp Ala Pro Gly His Glu Pro Gly Gly Ser Pro Gln Asp
50   260   265   270
        Glu Leu Asp Phe Ser Ile Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn
                        275   280   285
        Glu Glu Glu Pro Asn Ala His Lys Val Ala Ser Pro Pro Ser Gly Pro
55   290   295   300
        Ala Tyr Pro Asp Asp Val Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro

```
      305                     310                     315                     320
      Leu Ala Ser Leu Ser Gly Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp
                      325                     330                     335
      Arg Val Gly Pro Gln Lys Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala
  5                   340                     345                     350
      Ser Gly Leu Ser Pro Arg Ile Glu Ile Thr Pro Ser His Glu Leu Ile
                      355                     360                     365
      Gln Ala Val Gly Pro Leu Arg Met Arg Asp Ala Gly Leu Leu Val Glu
                      370                     375                     380
 10   Gln Pro Pro Leu Ala Gly Val Ala Ala Ser Pro Arg Phe Thr Leu Pro
      385                     390                     395                     400
      Val Pro Gly Phe Glu Gly Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala
                              405                     410                     415
      Ser Ser Gly Ser Ser Ala Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr
 15                   420                     425                     430
      Thr Ser Pro Cys Val Ser Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys
                      435                     440                     445
      Pro Gln Phe Gln Asn Ile Pro Ala His Tyr Ser Pro Arg Thr Ser Pro
                      450                     455                     460
 20   Ile Met Ser Pro Arg Thr Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg
      465                     470                     475                     480
      His Ser Pro Val Pro Arg Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala
                              485                     490                     495
      Lys Arg Arg His Ser Cys Ala Glu Ala Leu Val Ala Leu Pro Pro Gly
 25                   500                     505                     510
      Ala Ser Pro Gln Arg Ser Arg Ser Pro Ser Pro Gln Pro Ser Ser His
                      515                     520                     525
      Val Ala Pro Gln Asp His Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala
                      530                     535                     540
 30   Gly Ser Ala Val Ile Met Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser
      545                     550                     555                     560
      Pro Cys Gly Ile Pro Pro Lys Met Trp Lys Thr Ser Pro Asp Pro Ser
                              565                     570                     575
      Pro Val Ser Ala Ala Pro Ser Lys Ala Gly Leu Pro Arg His Ile Tyr
 35                   580                     585                     590
      Pro Ala Val Glu Phe Leu Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn
                      595                     600                     605
      Ser Ala Pro Glu Ser Ile Leu Leu Val Pro Pro Thr Trp Pro Lys Pro
                      610                     615                     620
 40   Leu Val Pro Ala Ile Pro Ile Cys Ser Ile Pro Val Thr Ala Ser Leu
      625                     630                     635                     640
      Pro Pro Leu Glu Trp Pro Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu
                      645                     650                     655
      Arg Ile Glu Val Gln Pro Lys Pro His His Arg Ala His Tyr Glu Thr
 45                   660                     665                     670
      Glu Gly Ser Arg Gly Ala Val Lys Ala Pro Thr Gly Gly His Pro Val
                      675                     680                     685
      Val Gln Leu His Gly Tyr Met Glu Asn Lys Pro Leu Gly Leu Gln Ile
                      690                     695                     700
 50   Phe Ile Gly Thr Ala Asp Glu Arg Ile Leu Lys Pro His Ala Phe Tyr
      705                     710                     715                     720
      Gln Val His Arg Ile Thr Gly Lys Thr Val Thr Thr Thr Ser Tyr Glu
                      725                     730                     735
      Lys Ile Val Gly Asn Thr Lys Val Leu Glu Ile Pro Leu Glu Pro Lys
 55                   740                     745                     750
      Asn Asn Met Arg Ala Thr Ile Asp Cys Ala Gly Ile Leu Lys Leu Arg
```

SUBSTITUTE SHEET (RULE 26)

```
            755                   760                   765
    Asn Ala Asp Ile Glu Leu Arg Lys Gly Glu Thr Asp Ile Gly Arg Lys
            770                   775                   780
    Asn Thr Arg Val Arg Leu Val Phe Arg Val His Ile Pro Glu Ser Ser
5   785                   790                   795                   800
    Gly Arg Ile Val Ser Leu Gln Thr Ala Ser Asn Pro Ile Glu Cys Ser
                    805                   810                   815
    Gln Arg Ser Ala His Glu Leu Pro Met Val Glu Arg Gln Asp Thr Asp
10                  820                   825                   830
    Ser Cys Leu Val Tyr Gly Gly Gln Gln Met Ile Leu Thr Gly Gln Asn
                    835                   840                   845
    Phe Thr Ser Glu Ser Lys Val Val Phe Thr Glu Lys Thr Thr Asp Gly
                    850                   855                   860
    Gln Gln Ile Trp Glu Met Glu Ala Thr Val Asp Lys Asp Lys Ser Gln
15  865                   870                   875                   880
    Pro Asn Met Leu Phe Val Glu Ile Pro Glu Tyr Arg Asn Lys His Ile
                    885                   890                   895
    Arg Thr Pro Val Lys Val Asn Phe Tyr Val Ile Asn Gly Lys Arg Lys
                    900                   905                   910
    Arg Ser Gln Pro Gln His Phe Thr Tyr His Pro Val Pro Ala Ile Lys
20                  915                   920                   925
    Thr Glu Pro Thr Asp Glu Tyr Asp Pro Thr Leu Ile Cys Ser Pro Thr
                    930                   935                   940
    His Gly Gly Leu Gly Ser Gln Pro Tyr Tyr Pro Gln His Pro Met Val
25  945                   950                   955                   960
    Ala Glu Ser Pro Ser Cys Leu Val Ala Thr Met Ala Pro Cys Gln Gln
                    965                   970                   975
    Phe Arg Thr Gly Leu Ser Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn
                    980                   985                   990
30  Pro Ala Ala Val Leu Tyr Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu
                    995                   1000                  1005
    Leu Gly Tyr Gln Gln Pro Ala Leu Met Ala Ala Pro Leu Ser Leu Ala
            1010                  1015                  1020
    Asp Ala His Arg Ser Val Leu Val His Ala Gly Ser Gln Gly Gln Ser
35  025                   1030                  1035                  1040
    Ser Ala Leu Leu His Pro Ser Pro Thr Asn Gln Gln Ala Ser Pro Val
                    1045                  1050                  1055
    Ile His Tyr Ser Pro Thr Asn Gln Gln Leu Arg Cys Gly Ser His Gln
                    1060                  1065                  1070
40  Glu Phe Gln His Ile Met Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr
            1075                  1080                  1085
    Arg Pro Gly Pro Pro Pro Val Ser Gln Gly Gln Arg Leu Ser Pro Gly
            1090                  1095                  1100
    Ser Tyr Pro Thr Val Ile Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala
45  105                   1110                  1115                  1120
    Ala Lys Asn Gly Pro Pro Val Ser Asp Gln Lys Glu Val Leu Pro Ala
                    1125                  1130                  1135
    Gly Val Thr Ile Lys Gln Glu Gln Asn Leu Asp Gln Thr Tyr Leu Asp
                    1140                  1145                  1150
50  Asp Val Asn Glu Ile Ile Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg
            1155                  1160                  1165
    Asn Gln Thr
            1170
```

55   (2) INFORMATION FOR SEQ ID NO:132:

```
        (i) SEQUENCE CHARACTERISTICS:
           (A) LENGTH: 3546 base pairs
           (B) TYPE: nucleic acid
           (C) STRANDEDNESS: single
5          (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: cDNA
        (ix) FEATURE:

10             (A) NAME/KEY: Coding Sequence
               (B) LOCATION: 1...3543
               (D) OTHER INFORMATION:

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:
15
    ATG AAC GCC CCC GAG CGG CAG CCC CAA CCC GAC GGC GGG GAC GCC CCA      48
    Met Asn Ala Pro Glu Arg Gln Pro Gln Pro Asp Gly Gly Asp Ala Pro
    1               5                   10                  15

20  GGC CAC GAG CCT GGG GGC AGC CCC CAA GAC GAG CTT GAC TTC TCC ATC      96
    Gly His Glu Pro Gly Gly Ser Pro Gln Asp Glu Leu Asp Phe Ser Ile
                    20                  25                  30

    CTC TTC GAC TAT GAG TAT TTG AAT CCG AAC GAA GAA GAG CCG AAT GCA     144
25  Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn Glu Glu Glu Pro Asn Ala
                35                  40                  45

    CAT AAG GTC GCC AGC CCA CCC TCC GGA CCC GCA TAC CCC GAT GAT GTA     192
    His Lys Val Ala Ser Pro Pro Ser Gly Pro Ala Tyr Pro Asp Asp Val
30      50                  55                  60

    ATG GAC TAT GGC CTC AAG CCA TAC AGC CCC CTT GCT AGT CTC TCT GGC     240
    Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro Leu Ala Ser Leu Ser Gly
    65                  70                  75                  80
35
    GAG CCC CCC GGC CGA TTC GGA GAG CCG GAT AGG GTA GGG CCG CAG AAG     288
    Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp Arg Val Gly Pro Gln Lys
                    85                  90                  95

40  TTT CTG AGC GCG GCC AAG CCA GCA GGG GCC TCG GGC CTG AGC CCT CGG     336
    Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala Ser Gly Leu Ser Pro Arg
                    100                 105                 110

    ATC GAG ATC ACT CCG TCC CAC GAA CTG ATC CAG GCA GTG GGG CCC CTC     384
45  Ile Glu Ile Thr Pro Ser His Glu Leu Ile Gln Ala Val Gly Pro Leu
                    115                 120                 125

    CGC ATG AGA GAC GCG GGC CTC CTG GTG GAG CAG CCT CCC CTG GCC GGG     432
    Arg Met Arg Asp Ala Gly Leu Leu Val Glu Gln Pro Pro Leu Ala Gly
50      130                 135                 140

    GTG GCC GCC AGC CCG AGG TTC ACC CTG CCC GTG CCC GGC TTC GAG GGC     480
    Val Ala Ala Ser Pro Arg Phe Thr Leu Pro Val Pro Gly Phe Glu Gly
    145                 150                 155                 160
55
    TAC CGC GAG CCG CTT TGC TTG AGC CCC GCT AGC AGC GGC TCC TCT GCC     528
```
                                                                          261

SUBSTITUTE SHEET (RULE 26)

262

```
          Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala Ser Ser Gly Ser Ser Ala
                          165             170             175

  5       AGC TTC ATT TCT GAC ACC TTC TCC CCC TAC ACC TCG CCC TGC GTC TCG   576
          Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr Thr Ser Pro Cys Val Ser
                          180             185             190

          CCC AAT AAC GGC GGG CCC GAC GAC CTG TGT CCG CAG TTT CAA AAC ATC   624
          Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys Pro Gln Phe Gln Asn Ile
 10                       195             200             205

          CCT GCT CAT TAT TCC CCC AGA ACC TCG CCA ATA ATG TCA CCT CGA ACC   672
          Pro Ala His Tyr Ser Pro Arg Thr Ser Pro Ile Met Ser Pro Arg Thr
                  210             215             220
 15
          AGC CTC GCC GAG GAC AGC TGC CTG GGC CGC CAC TCG CCC GTG CCC CGT   720
          Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg His Ser Pro Val Pro Arg
          225             230             235             240

 20       CCG GCC TCC CGC TCC TCA TCG CCT GGT GCC AAG CGG AGG CAT TCG TGC   768
          Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala Lys Arg Arg His Ser Cys
                          245             250             255

          GCC GAG GCC TTG GTT GCC CTG CCG CCC GGA GCC TCA CCC CAG CGC TCC   816
 25       Ala Glu Ala Leu Val Ala Leu Pro Pro Gly Ala Ser Pro Gln Arg Ser
                          260             265             270

          CGG AGC CCC TCG CCG CAG CCC TCA TCT CAC GTG GCA CCC CAG GAC CAC   864
          Arg Ser Pro Ser Pro Gln Pro Ser Ser His Val Ala Pro Gln Asp His
 30               275             280             285

          GGC TCC CCG GCT GGG TAC CCC CCT GTG GCT GGC TCT GCC GTG ATC ATG   912
          Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala Gly Ser Ala Val Ile Met
                  290             295             300
 35
          GAT GCC CTG AAC AGC CTC GCC ACG GAC TCG CCT TGT GGG ATC CCC CCC   960
          Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser Pro Cys Gly Ile Pro Pro
          305             310             315             320

 40       AAG ATG TGG AAG ACC AGC CCT GAC CCC TCG CCG GTG TCT GCC GCC CCA  1008
          Lys Met Trp Lys Thr Ser Pro Asp Pro Ser Pro Val Ser Ala Ala Pro
                          325             330             335

          TCC AAG GCC GGC CTG CCT CGC CAC ATC TAC CCG GCC GTG GAG TTC CTG  1056
 45       Ser Lys Ala Gly Leu Pro Arg His Ile Tyr Pro Ala Val Glu Phe Leu
                          340             345             350

          GGG CCC TGC GAG CAG GGC GAG AGG AGA AAC TCG GCT CCA GAA TCC ATC  1104
          Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn Ser Ala Pro Glu Ser Ile
 50               355             360             365

          CTG CTG GTT CCG CCC ACT TGG CCC AAG CCG CTG GTG CCT GCC ATT CCC  1152
          Leu Leu Val Pro Pro Thr Trp Pro Lys Pro Leu Val Pro Ala Ile Pro
                  370             375             380
 55
          ATC TGC AGC ATC CCA GTG ACT GCA TCC CTC CCT CCA CTT GAG TGG CCG  1200
```
                                                                         262

SUBSTITUTE SHEET (RULE 26)

```
     Ile Cys Ser Ile Pro Val Thr Ala Ser Leu Pro Pro Leu Glu Trp Pro
     385             390             395             400

 5   CTG TCC AGT CAG TCA GGC TCT TAC GAG CTG CGG ATC GAG GTG CAG CCC    -1248
     Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu Arg Ile Glu Val Gln Pro
                     405             410             415

     AAG CCA CAT CAC CGG GCC CAC TAT GAG ACA GAA GGC AGC CGA GGG GCT    1296
10   Lys Pro His His Arg Ala His Tyr Glu Thr Glu Gly Ser Arg Gly Ala
                 420             425             430

     GTC AAA GCT CCA ACT GGA GGC CAC CCT GTG GTT CAG CTC CAT GGC TAC    1344
     Val Lys Ala Pro Thr Gly Gly His Pro Val Val Gln Leu His Gly Tyr
                 435             440             445
15
     ATG GAA AAC AAG CCT CTG GGA CTT CAG ATC TTC ATT GGG ACA GCT GAT    1392
     Met Glu Asn Lys Pro Leu Gly Leu Gln Ile Phe Ile Gly Thr Ala Asp
             450             455             460

20   GAG CGG ATC CTT AAG CCG CAC GCC TTC TAC CAG GTG CAC CGA ATC ACG    1440
     Glu Arg Ile Leu Lys Pro His Ala Phe Tyr Gln Val His Arg Ile Thr
     465             470             475             480

     GGG AAA ACT GTC ACC ACC ACC AGC TAT GAG AAG ATA GTG GGC AAC ACC    1488
25   Gly Lys Thr Val Thr Thr Thr Ser Tyr Glu Lys Ile Val Gly Asn Thr
                     485             490             495

     AAA GTC CTG GAG ATC CCC TTG GAG CCC AAA AAC AAC ATG AGG GCA ACC    1536
     Lys Val Leu Glu Ile Pro Leu Glu Pro Lys Asn Asn Met Arg Ala Thr
30               500             505             510

     ATC GAC TGT GCG GGG ATC TTG AAG CTT AGA AAC GCC GAC ATT GAG CTG    1584
     Ile Asp Cys Ala Gly Ile Leu Lys Leu Arg Asn Ala Asp Ile Glu Leu
                 515             520             525
35
     CGG AAA GGC GAG ACG GAC ATT GGA AGA AAG AAC ACG CGG GTG AGA CTG    1632
     Arg Lys Gly Glu Thr Asp Ile Gly Arg Lys Asn Thr Arg Val Arg Leu
                 530             535             540

40   GTT TTC CGA GTT CAC ATC CCA GAG TCC AGT GGC AGA ATC GTC TCT TTA    1680
     Val Phe Arg Val His Ile Pro Glu Ser Ser Gly Arg Ile Val Ser Leu
     545             550             555             560

     CAG ACT GCA TCT AAC CCC ATC GAG TGC TCC CAG CGA TCT GCT CAC GAG    1728
45   Gln Thr Ala Ser Asn Pro Ile Glu Cys Ser Gln Arg Ser Ala His Glu
                     565             570             575

     CTG CCC ATG GTT GAA AGA CAA GAC ACA GAC AGC TGC CTG GTC TAT GGC    1776
     Leu Pro Met Val Glu Arg Gln Asp Thr Asp Ser Cys Leu Val Tyr Gly
50               580             585             590

     GGC CAG CAA ATG ATC CTC ACG GGG CAG AAC TTT ACA TCC GAG TCC AAA    1824
     Gly Gln Gln Met Ile Leu Thr Gly Gln Asn Phe Thr Ser Glu Ser Lys
                 595             600             605
55
     GTT GTG TTT ACT GAG AAG ACC ACA GAT GGA CAG CAA ATT TGG GAG ATG    1872
```

263

SUBSTITUTE SHEET (RULE 26)

264

```
        Val Val Phe Thr Glu Lys Thr Thr Asp Gly Gln Gln Ile Trp Glu Met
            610             615             620

 5      GAA GCC ACG GTG GAT AAG GAC AAG AGC CAG CCC AAC ATG CTT TTT GTT      1920
        Glu Ala Thr Val Asp Lys Asp Lys Ser Gln Pro Asn Met Leu Phe Val
        625             630             635             640

10      GAG ATC CCT GAA TAT CGG AAC AAG CAT ATC CGC ACA CCT GTA AAA GTG      1968
        Glu Ile Pro Glu Tyr Arg Asn Lys His Ile Arg Thr Pro Val Lys Val
                        645             650             655

        AAC TTC TAC GTC ATC AAT GGG AAG AGA AAA CGA AGT CAG CCT CAG CAC      2016
        Asn Phe Tyr Val Ile Asn Gly Lys Arg Lys Arg Ser Gln Pro Gln His
                    660             665             670
15

        TTT ACC TAC CAC CCA GTC CCA GCC ATC AAG ACG GAG CCC ACG GAT GAA      2064
        Phe Thr Tyr His Pro Val Pro Ala Ile Lys Thr Glu Pro Thr Asp Glu
                    675             680             685

20      TAT GAC CCC ACT CTG ATC TGC AGC CCC ACC CAT GGA GGC CTG GGG AGC      2112
        Tyr Asp Pro Thr Leu Ile Cys Ser Pro Thr His Gly Gly Leu Gly Ser
                690             695             700

        CAG CCT TAC TAC CCC CAG CAC CCG ATG GTG GCC GAG TCC CCC TCC TGC      2160
25      Gln Pro Tyr Tyr Pro Gln His Pro Met Val Ala Glu Ser Pro Ser Cys
        705             710             715             720

        CTC GTG GCC ACC ATG GCT CCC TGC CAG CAG TTC CGC ACG GGG CTC TCA      2208
        Leu Val Ala Thr Met Ala Pro Cys Gln Gln Phe Arg Thr Gly Leu Ser
30                      725             730             735

        TCC CCT GAC GCC CGC TAC CAG CAA CAG AAC CCA GCG GCC GTA CTC TAC      2256
        Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn Pro Ala Ala Val Leu Tyr
                    740             745             750
35

        CAG CGG AGC AAG AGC CTG AGC CCC AGC CTG CTG GGC TAT CAG CAG CCG      2304
        Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu Leu Gly Tyr Gln Gln Pro
                    755             760             765

40      GCC CTC ATG GCC GCC CCG CTG TCC CTT GCG GAC GCT CAC CGC TCT GTG      2352
        Ala Leu Met Ala Ala Pro Leu Ser Leu Ala Asp Ala His Arg Ser Val
                770             775             780

        CTG GTG CAC GCC GGC TCC CAG GGC CAG AGC TCA GCC CTG CTC CAC CCC      2400
45      Leu Val His Ala Gly Ser Gln Gly Gln Ser Ser Ala Leu Leu His Pro
        785             790             795             800

        TCT CCG ACC AAC CAG CAG GCC TCG CCT GTG ATC CAC TAC TCA CCC ACC      2448
        Ser Pro Thr Asn Gln Gln Ala Ser Pro Val Ile His Tyr Ser Pro Thr
                        805             810             815
50

        AAC CAG CAG CTG CGC TGC GGA AGC CAC CAG GAG TTC CAG CAC ATC ATG      2496
        Asn Gln Gln Leu Arg Cys Gly Ser His Gln Glu Phe Gln His Ile Met
                    820             825             830
55

        TAC TGC GAG AAT TTC GCA CCA GGC ACC ACC AGA CCT GGC CCG CCC CCG      2544
```

264

SUBSTITUTE SHEET (RULE 26)

265

```
          Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr Arg Pro Gly Pro Pro Pro
                  835                 840                 845

 5        GTC AGT CAA GGT CAG AGG CTG AGC CCG GGT TCC TAC CCC ACA GTC ATT    2592
          Val Ser Gln Gly Gln Arg Leu Ser Pro Gly Ser Tyr Pro Thr Val Ile
                  850                 855                 860

          CAG CAG CAG AAT GCC ACG AGC CAA AGA GCC GCC AAA AAC GGA CCC CCG    2640
          Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala Ala Lys Asn Gly Pro Pro
 10       865                 870                 875                 880

          GTC AGT GAC CAA AAG GAA GTA TTA CCT GCG GGG GTG ACC ATT AAA CAG    2688
          Val Ser Asp Gln Lys Glu Val Leu Pro Ala Gly Val Thr Ile Lys Gln
                          885                 890                 895
 15
          GAG CAG AAC TTG GAC CAG ACC TAC TTG GAT GAT GTT AAT GAA ATT ATC    2736
          Glu Gln Asn Leu Asp Gln Thr Tyr Leu Asp Asp Val Asn Glu Ile Ile
                  900                 905                 910

 20       AGG AAG GAG TTT TCA GGA CCT CCT GCC AGA AAT CAG ACG AGA ATT CTG    2784
          Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg Asn Gln Thr Arg Ile Leu
                  915                 920                 925

          CAG TCG ACG GTA CCG CGG GCC CGG GAT CCA CCG GTC GCC ACC ATG GTG    2832
 25       Gln Ser Thr Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met Val
                  930                 935                 940

          AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG    2880
          Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
 30       945                 950                 955                 960

          CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC    2928
          Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly
                          965                 970                 975
 35
          GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC    2976
          Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
                  980                 985                 990

 40       ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC    3024
          Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
                  995                 1000                1005

          TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC    3072
 45       Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
                  1010                1015                1020

          GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC    3120
          Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
 50       1025                1030                1035                1040

          ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG    3168
          Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
                          1045                1050                1055
 55
          TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC    3216
```

```
      Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
              1060                1065                1070


      TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC    3264
 5    Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
              1075                1080                1085

      AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC    3312
      Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
 10      1090                1095                1100

      AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG    3360
      Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
      1105                1110                1115                1120
 15

      CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG    3408
      Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                 1125                1130                1135

 20   CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA    3456
      Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
                 1140                1145                1150

      GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC    3504
 25   Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
                 1155                1160                1165

      GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA            3546
      Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
 30      1170                1175                1180


              (2)  INFORMATION FOR SEQ ID NO:133:

 35           (i)  SEQUENCE CHARACTERISTICS:
                   (A)  LENGTH: 1181 amino acids
                   (B)  TYPE: amino acid
                   (C)  STRANDEDNESS: single
                   (D)  TOPOLOGY: linear
 40
              (ii) MOLECULE TYPE: protein
              (v)  FRAGMENT TYPE: internal

              (xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:
 45
      Met Asn Ala Pro Glu Arg Gln Pro Gln Pro Asp Gly Gly Asp Ala Pro
       1               5                10                15
      Gly His Glu Pro Gly Gly Ser Pro Gln Asp Glu Leu Asp Phe Ser Ile
                  20                25                30
 50   Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn Glu Glu Glu Pro Asn Ala
                  35                40                45
      His Lys Val Ala Ser Pro Pro Ser Gly Pro Ala Tyr Pro Asp Asp Val
              50                55                60
      Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro Leu Ala Ser Leu Ser Gly
 55   65                70                75                80
      Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp Arg Val Gly Pro Gln Lys
```

```
                        85                    90                         95
     Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala Ser Gly Leu Ser Pro Arg
                     100                   105                   110
     Ile Glu Ile Thr Pro Ser His Glu Leu Ile Gln Ala Val Gly Pro Leu
 5                   115                   120                   125
     Arg Met Arg Asp Ala Gly Leu Leu Val Glu Gln Pro Pro Leu Ala Gly
                 130                   135                   140
     Val Ala Ala Ser Pro Arg Phe Thr Leu Pro Val Pro Gly Phe Glu Gly
     145                   150                   155                   160
10   Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala Ser Ser Gly Ser Ser Ala
                         165                   170                   175
     Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr Thr Ser Pro Cys Val Ser
                     180                   185                   190
     Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys Pro Gln Phe Gln Asn Ile
15                   195                   200                   205
     Pro Ala His Tyr Ser Pro Arg Thr Ser Pro Ile Met Ser Pro Arg Thr
                 210                   215                   220
     Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg His Ser Pro Val Pro Arg
     225                   230                   235                   240
20   Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala Lys Arg Arg His Ser Cys
                         245                   250                   255
     Ala Glu Ala Leu Val Ala Leu Pro Pro Gly Ala Ser Pro Gln Arg Ser
                     260                   265                   270
     Arg Ser Pro Ser Pro Gln Pro Ser Ser His Val Ala Pro Gln Asp His
25                   275                   280                   285
     Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala Gly Ser Ala Val Ile Met
                 290                   295                   300
     Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser Pro Cys Gly Ile Pro Pro
     305                   310                   315                   320
30   Lys Met Trp Lys Thr Ser Pro Asp Pro Ser Pro Val Ser Ala Ala Pro
                         325                   330                   335
     Ser Lys Ala Gly Leu Pro Arg His Ile Tyr Pro Ala Val Glu Phe Leu
                     340                   345                   350
     Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn Ser Ala Pro Glu Ser Ile
35                   355                   360                   365
     Leu Leu Val Pro Pro Thr Trp Pro Lys Pro Leu Val Pro Ala Ile Pro
                 370                   375                   380
     Ile Cys Ser Ile Pro Val Thr Ala Ser Leu Pro Pro Leu Glu Trp Pro
     385                   390                   395                   400
40   Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu Arg Ile Glu Val Gln Pro
                         405                   410                   415
     Lys Pro His His Arg Ala His Tyr Glu Thr Glu Gly Ser Arg Gly Ala
                     420                   425                   430
     Val Lys Ala Pro Thr Gly Gly His Pro Val Val Gln Leu His Gly Tyr
45                   435                   440                   445
     Met Glu Asn Lys Pro Leu Gly Leu Gln Ile Phe Ile Gly Thr Ala Asp
                 450                   455                   460
     Glu Arg Ile Leu Lys Pro His Ala Phe Tyr Gln Val His Arg Ile Thr
     465                   470                   475                   480
50   Gly Lys Thr Val Thr Thr Thr Ser Tyr Glu Lys Ile Val Gly Asn Thr
                         485                   490                   495
     Lys Val Leu Glu Ile Pro Leu Glu Pro Lys Asn Asn Met Arg Ala Thr
                     500                   505                   510
     Ile Asp Cys Ala Gly Ile Leu Lys Leu Arg Asn Ala Asp Ile Glu Leu
55                   515                   520                   525
     Arg Lys Gly Glu Thr Asp Ile Gly Arg Lys Asn Thr Arg Val Arg Leu
```

```
            530                    535                    540
     Val Phe Arg Val His Ile Pro Glu Ser Ser Gly Arg Ile Val Ser Leu
     545                    550                    555                    560
     Gln Thr Ala Ser Asn Pro Ile Glu Cys Ser Gln Arg Ser Ala His Glu
  5                         565                    570                    575
     Leu Pro Met Val Glu Arg Gln Asp Thr Asp Ser Cys Leu Val Tyr Gly
                        580                    585                    590
     Gly Gln Gln Met Ile Leu Thr Gly Gln Asn Phe Thr Ser Glu Ser Lys
                        595                    600                    605
 10  Val Val Phe Thr Glu Lys Thr Thr Asp Gly Gln Gln Ile Trp Glu Met
         610                    615                    620
     Glu Ala Thr Val Asp Lys Asp Lys Ser Gln Pro Asn Met Leu Phe Val
     625                    630                    635                    640
     Glu Ile Pro Glu Tyr Arg Asn Lys His Ile Arg Thr Pro Val Lys Val
 15                     645                    650                    655
     Asn Phe Tyr Val Ile Asn Gly Lys Arg Lys Arg Ser Gln Pro Gln His
                        660                    665                    670
     Phe Thr Tyr His Pro Val Pro Ala Ile Lys Thr Glu Pro Thr Asp Glu
                    675                    680                    685
 20  Tyr Asp Pro Thr Leu Ile Cys Ser Pro Thr His Gly Gly Leu Gly Ser
         690                    695                    700
     Gln Pro Tyr Tyr Pro Gln His Pro Met Val Ala Glu Ser Pro Ser Cys
     705                    710                    715                    720
     Leu Val Ala Thr Met Ala Pro Cys Gln Gln Phe Arg Thr Gly Leu Ser
 25                     725                    730                    735
     Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn Pro Ala Ala Val Leu Tyr
                        740                    745                    750
     Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu Leu Gly Tyr Gln Gln Pro
                    755                    760                    765
 30  Ala Leu Met Ala Ala Pro Leu Ser Leu Ala Asp Ala His Arg Ser Val
         770                    775                    780
     Leu Val His Ala Gly Ser Gln Gly Gln Ser Ser Ala Leu Leu His Pro
     785                    790                    795                    800
     Ser Pro Thr Asn Gln Gln Ala Ser Pro Val Ile His Tyr Ser Pro Thr
 35                     805                    810                    815
     Asn Gln Gln Leu Arg Cys Gly Ser His Gln Glu Phe Gln His Ile Met
                        820                    825                    830
     Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr Arg Pro Gly Pro Pro Pro
                    835                    840                    845
 40  Val Ser Gln Gly Gln Arg Leu Ser Pro Gly Ser Tyr Pro Thr Val Ile
         850                    855                    860
     Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala Ala Lys Asn Gly Pro Pro
     865                    870                    875                    880
     Val Ser Asp Gln Lys Glu Val Leu Pro Ala Gly Val Thr Ile Lys Gln
 45                     885                    890                    895
     Glu Gln Asn Leu Asp Gln Thr Tyr Leu Asp Asp Val Asn Glu Ile Ile
                        900                    905                    910
     Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg Asn Gln Thr Arg Ile Leu
                    915                    920                    925
 50  Gln Ser Thr Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met Val
         930                    935                    940
     Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
     945                    950                    955                    960
     Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly
 55                     965                    970                    975
     Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
```

268

BNSDOCID <WO   9845704A2 I >

```
                 980              985                990
     Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
                 995             1000               1005
     Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
5        1010            1015               1020
     Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
         025             1030               1035               1040
     Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
                 1045            1050               1055
10   Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
                 1060            1065               1070
     Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
             1075                1080               1085
     Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
15       1090            1095               1100
     Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
         105             1110               1115               1120
     Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                 1125            1130               1135
20   Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
             1140                1145               1150
     Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
             1155                1160               1165
     Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
25       1170            1175               1180
```

          (2) INFORMATION FOR SEQ ID NO:134:

          (i) SEQUENCE CHARACTERISTICS:
30   (A) LENGTH: 2802 base pairs
              (B) TYPE: nucleic acid
              (C) STRANDEDNESS: single
              (D) TOPOLOGY: linear

35   (ii) MOLECULE TYPE: cDNA
          (ix) FEATURE:

              (A) NAME/KEY: Coding Sequence
              (B) LOCATION: 1...2799
40   (D) OTHER INFORMATION:

          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

```
     ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG     48
45   Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                   10                  15


     GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC     96
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
50               20                  25                  30


     GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC    144
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                 35                  40                  45
55
     TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC    192
```

270

```
          Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
              50              55              60

   5      CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG    240
          Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
          65              70              75              80

          CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG    288
          Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
  10                      85              90              95

          CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG    336
          Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                      100             105             110
  15
          GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC    384
          Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                      115             120             125

  20      ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC    432
          Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                      130             135             140

          AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC    480
  25      Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
          145             150             155             160

          GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC    528
          Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
  30                      165             170             175

          GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC    576
          Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                      180             185             190
  35
          CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
          Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                      195             200             205

  40      AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
          Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                      210             215             220

          GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
  45      Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
          225             230             235             240

          GGA CTC AGA TCT CGA GGG AGC ATG GGC ACC TTG CGG GAT TTA CAG TAC    768
          Gly Leu Arg Ser Arg Gly Ser Met Gly Thr Leu Arg Asp Leu Gln Tyr
  50                      245             250             255

          GCG CTC CAG GAG AAG ATC GAG GAG CTG AGG CAG CGG GAT GCT CTC ATC    816
          Ala Leu Gln Glu Lys Ile Glu Glu Leu Arg Gln Arg Asp Ala Leu Ile
                      260             265             270
  55
          GAC GAG CTG GAG CTG GAG TTG GAT CAG AAG GAC GAA CTG ATC CAG AAG    864
                                                                          270
```

```
          Asp Glu Leu Glu Leu Glu Leu Asp Gln Lys Asp Glu Leu Ile Gln Lys
                  275                 280                 285

  5       CTG CAG AAC GAG CTG GAC AAG TAC CGC TCG GTG ATC CGA CCA GCC ACC      912
          Leu Gln Asn Glu Leu Asp Lys Tyr Arg Ser Val Ile Arg Pro Ala Thr
                  290                 295                 300

          CAG CAG GCG CAG AAG CAG AGC GCG AGC ACC TTG CAG GGC GAG CCG CGC      960
          Gln Gln Ala Gln Lys Gln Ser Ala Ser Thr Leu Gln Gly Glu Pro Arg
 10       305                 310                 315                 320

          ACC AAG CGG CAG GCG ATC TCC GCC GAG CCC ACC GCC TTC GAC ATC CAG     1008
          Thr Lys Arg Gln Ala Ile Ser Ala Glu Pro Thr Ala Phe Asp Ile Gln
                          325                 330                 335
 15
          GAT CTC AGC CAT GTG ACC CTG CCC TTC TAC CCC AAG AGC CCA CAG TCC     1056
          Asp Leu Ser His Val Thr Leu Pro Phe Tyr Pro Lys Ser Pro Gln Ser
                          340                 345                 350

 20       AAG GAT CTT ATA AAG GAA GCT ATC CTT GAC AAT GAC TTT ATG AAG AAC     1104
          Lys Asp Leu Ile Lys Glu Ala Ile Leu Asp Asn Asp Phe Met Lys Asn
                          355                 360                 365

          TTG GAG CTG TCG CAG ATC CAG GAG ATT GTG GAT TGT ATG TAC CCG GTG     1152
 25       Leu Glu Leu Ser Gln Ile Gln Glu Ile Val Asp Cys Met Tyr Pro Val
                  370                 375                 380

          GAG TAT GGC AAG GAC AGT TGC ATC ATC AAA GAA GGA GAC GTG GGG TCA     1200
          Glu Tyr Gly Lys Asp Ser Cys Ile Ile Lys Glu Gly Asp Val Gly Ser
 30       385                 390                 395                 400

          CTG GTG TAT GTC ATG GAA GAT GGT AAG GTT GAA GTT ACA AAA GAA GGT     1248
          Leu Val Tyr Val Met Glu Asp Gly Lys Val Glu Val Thr Lys Glu Gly
                          405                 410                 415
 35
          GTG AAG TTG TGT ACC ATG GGT CCA GGA AAA GTG TTT GGG GAA TTG GCT     1296
          Val Lys Leu Cys Thr Met Gly Pro Gly Lys Val Phe Gly Glu Leu Ala
                  420                 425                 430

 40       ATT CTT TAC AAC TGT ACC CGG ACA GCG ACC GTC AAG ACT CTT GTA AAT     1344
          Ile Leu Tyr Asn Cys Thr Arg Thr Ala Thr Val Lys Thr Leu Val Asn
                  435                 440                 445

          GTA AAA CTC TGG GCC ATT GAT CGA CAA TGT TTT CAA ACA ATA ATG ATG     1392
 45       Val Lys Leu Trp Ala Ile Asp Arg Gln Cys Phe Gln Thr Ile Met Met
                  450                 455                 460

          AGG ACA GGA CTC ATC AAG CAT ACC GAG TAT ATG GAA TTT TTA AAA AGC     1440
          Arg Thr Gly Leu Ile Lys His Thr Glu Tyr Met Glu Phe Leu Lys Ser
 50       465                 470                 475                 480

          GTT CCA ACA TTC CAG AGC CTT CCT GAA GAG ATC CTC AGC AAG CTT GCT     1488
          Val Pro Thr Phe Gln Ser Leu Pro Glu Glu Ile Leu Ser Lys Leu Ala
                          485                 490                 495
 55
          GAT GTC CTT GAA GAG ACC CAC TAT GAA AAT GGA GAA TAT ATT ATC AGG     1536
```

271

SUBSTITUTE SHEET (RULE 26)

```
          Asp Val Leu Glu Glu Thr His Tyr Glu Asn Gly Glu Tyr Ile Ile Arg
                       500                 505                 510

  5       CAA GGT GCA AGA GGG GAC ACC TTC TTT ATC ATC AGC AAA GGA ACG GTA      1584
          Gln Gly Ala Arg Gly Asp Thr Phe Phe Ile Ile Ser Lys Gly Thr Val
                       515                 520                 525

          AAT GTC ACT CGT GAA GAC TCA CCG AGT GAA GAC CCA GTC TTT CTT AGA      1632
 10       Asn Val Thr Arg Glu Asp Ser Pro Ser Glu Asp Pro Val Phe Leu Arg
                   530                 535                 540

          ACT TTA GGA AAA GGA GAC TGG TTT GGA GAG AAA GCC TTG CAG GGG GAA      1680
          Thr Leu Gly Lys Gly Asp Trp Phe Gly Glu Lys Ala Leu Gln Gly Glu
              545                 550                 555                 560
 15
          GAT GTG AGA ACA GCA AAC GTA ATT GCT GCA GAA GCT GTA ACC TGC CTT      1728
          Asp Val Arg Thr Ala Asn Val Ile Ala Ala Glu Ala Val Thr Cys Leu
                       565                 570                 575

 20       GTG ATT GAC AGA GAC TCT TTT AAA CAT TTG ATT GGA GGG CTG GAT GAT      1776
          Val Ile Asp Arg Asp Ser Phe Lys His Leu Ile Gly Gly Leu Asp Asp
                       580                 585                 590

          GTT TCT AAT AAA GCA TAT GAA GAT GCA GAA GCT AAA GCA AAA TAT GAA      1824
 25       Val Ser Asn Lys Ala Tyr Glu Asp Ala Glu Ala Lys Ala Lys Tyr Glu
                   595                 600                 605

          GCT GAA GCG GCT TTC TTC GCC AAC CTG AAG CTG TCT GAT TTC AAC ATC      1872
          Ala Glu Ala Ala Phe Phe Ala Asn Leu Lys Leu Ser Asp Phe Asn Ile
 30           610                 615                 620

          ATT GAT ACC CTT GGA GTT GGA GGT TTC GGA CGA GTA GAA CTG GTC CAG      1920
          Ile Asp Thr Leu Gly Val Gly Gly Phe Gly Arg Val Glu Leu Val Gln
              625                 630                 635                 640
 35
          TTG AAA AGT GAA GAA TCC AAA ACG TTT GCA ATG AAG ATT CTC AAG AAA      1968
          Leu Lys Ser Glu Glu Ser Lys Thr Phe Ala Met Lys Ile Leu Lys Lys
                       645                 650                 655

 40       CGT CAC ATT GTG GAC ACA AGA CAG CAG GAG CAC ATC CGC TCA GAG AAG      2016
          Arg His Ile Val Asp Thr Arg Gln Gln Glu His Ile Arg Ser Glu Lys
                       660                 665                 670

          CAG ATC ATG CAG GGG GCT CAT TCC GAT TTC ATA GTG AGA CTG TAC AGA      2064
 45       Gln Ile Met Gln Gly Ala His Ser Asp Phe Ile Val Arg Leu Tyr Arg
                   675                 680                 685

          ACA TTT AAG GAC AGC AAA TAT TTG TAT ATG TTG ATG GAA GCT TGT CTA      2112
          Thr Phe Lys Asp Ser Lys Tyr Leu Tyr Met Leu Met Glu Ala Cys Leu
 50           690                 695                 700

          GGT GGA GAG CTC TGG ACC ATT CTC AGG GAT AGA GGT TCG TTT GAA GAT      2160
          Gly Gly Glu Leu Trp Thr Ile Leu Arg Asp Arg Gly Ser Phe Glu Asp
              705                 710                 715                 720
 55
          TCT ACA ACC AGA TTT TAC ACA GCA TGT GTG GTA GAA GCT TTT GCC TAT      2208
```

```
           Ser Thr Thr Arg Phe Tyr Thr Ala Cys Val Val Glu Ala Phe Ala Tyr
                       725             730             735

       CTG CAT TCC AAA GGA ATC ATT TAC AGG GAC CTC AAG CCA GAA AAT CTC   2256
    5  Leu His Ser Lys Gly Ile Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu
                   740             745             750

       ATC CTA GAT CAC CGA GGT TAT GCC AAA CTG GTT GAT TTT GGC TTT GCA   2304
   10  Ile Leu Asp His Arg Gly Tyr Ala Lys Leu Val Asp Phe Gly Phe Ala
                   755             760             765

       AAG AAA ATA GGA TTT GGA AAG AAA ACA TGG ACT TTT TGT GGG ACT CCA   2352
       Lys Lys Ile Gly Phe Gly Lys Lys Thr Trp Thr Phe Cys Gly Thr Pro
                   770             775             780
   15
       GAG TAT GTA GCC CCA GAG ATC ATC CTG AAC AAA GGC CAT GAC ATT TCA   2400
       Glu Tyr Val Ala Pro Glu Ile Ile Leu Asn Lys Gly His Asp Ile Ser
       785             790             795             800

   20  GCC GAC TAC TGG TCA CTG GGA ATC CTA ATG TAT GAA CTC CTG ACT GGC   2448
       Ala Asp Tyr Trp Ser Leu Gly Ile Leu Met Tyr Glu Leu Leu Thr Gly
                       805             810             815

       AGC CCA CCT TTC TCA GGC CCA GAT CCT ATG AAA ACC TAT AAC ATC ATA   2496
   25  Ser Pro Pro Phe Ser Gly Pro Asp Pro Met Lys Thr Tyr Asn Ile Ile
                   820             825             830

       TTG AGG GGG ATT GAC ATG ATA GAA TTT CCA AAG AAG ATT GCC AAA AAT   2544
       Leu Arg Gly Ile Asp Met Ile Glu Phe Pro Lys Lys Ile Ala Lys Asn
   30              835             840             845

       GCT GCT AAT TTA ATT AAA AAA CTA TGC AGG GAC AAT CCA TCA GAA AGA   2592
       Ala Ala Asn Leu Ile Lys Lys Leu Cys Arg Asp Asn Pro Ser Glu Arg
                   850             855             860
   35
       TTA GGG AAT TTG AAA AAT GGA GTA AAA GAC ATT CAA AAG CAC AAA TGG   2640
       Leu Gly Asn Leu Lys Asn Gly Val Lys Asp Ile Gln Lys His Lys Trp
       865             870             875             880

   40  TTT GAG GGC TTT AAC TGG GAA GGC TTA AGA AAA GGT ACC TTG ACA CCT   2688
       Phe Glu Gly Phe Asn Trp Glu Gly Leu Arg Lys Gly Thr Leu Thr Pro
                       885             890             895

       CCT ATA ATA CCA AGT GTT GCA TCA CCC ACA GAC ACA AGT AAT TTT GAC   2736
   45  Pro Ile Ile Pro Ser Val Ala Ser Pro Thr Asp Thr Ser Asn Phe Asp
                   900             905             910

       AGT TTC CCT GAG GAC AAC GAT GAA CCA CCA CCT GAT GAC AAC TCA GGA   2784
       Ser Phe Pro Glu Asp Asn Asp Glu Pro Pro Pro Asp Asp Asn Ser Gly
   50              915             920             925

       TGG GAT ATA GAC TTC TAA                                          2802
       Trp Asp Ile Asp Phe
                   930
   55
```

274

(2) INFORMATION FOR SEQ ID NO:135:

    (i) SEQUENCE CHARACTERISTICS:
      (A) LENGTH: 933 amino acids
5   (B) TYPE: amino acid
      (C) STRANDEDNESS: single
      (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: protein
10   (v) FRAGMENT TYPE: internal

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

```
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
15    1               5                  10                  15
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                     20                  25                  30
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                     35                  40                  45
20   Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                 50                  55                  60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
     65                  70                  75                  80
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
25                       85                  90                  95
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100                 105                 110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                115                 120                 125
30   Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
            130                 135                 140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                 150                 155                 160
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
35                   165                 170                 175
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                    180                 185                 190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                    195                 200                 205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
40               210                 215                 220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230                 235                 240
     Gly Leu Arg Ser Arg Gly Ser Met Gly Thr Leu Arg Asp Leu Gln Tyr
45                   245                 250                 255
     Ala Leu Gln Glu Lys Ile Glu Glu Leu Arg Gln Arg Asp Ala Leu Ile
                    260                 265                 270
     Asp Glu Leu Glu Leu Glu Leu Asp Gln Lys Asp Glu Leu Ile Gln Lys
                    275                 280                 285
50   Leu Gln Asn Glu Leu Asp Lys Tyr Arg Ser Val Ile Arg Pro Ala Thr
            290                 295                 300
     Gln Gln Ala Gln Lys Gln Ser Ala Ser Thr Leu Gln Gly Glu Pro Arg
     305                 310                 315                 320
     Thr Lys Arg Gln Ala Ile Ser Ala Glu Pro Thr Ala Phe Asp Ile Gln
55                   325                 330                 335
     Asp Leu Ser His Val Thr Leu Pro Phe Tyr Pro Lys Ser Pro Gln Ser
```

```
                    340                    345                    350
     Lys Asp Leu Ile Lys Glu Ala Ile Leu Asp Asn Asp Phe Met Lys Asn
             355                    360                    365
     Leu Glu Leu Ser Gln Ile Gln Glu Ile Val Asp Cys Met Tyr Pro Val
 5           370                    375                    380
     Glu Tyr Gly Lys Asp Ser Cys Ile Ile Lys Glu Gly Asp Val Gly Ser
     385                    390                    395                    400
     Leu Val Tyr Val Met Glu Asp Gly Lys Val Glu Val Thr Lys Glu Gly
                         405                    410                    415
10   Val Lys Leu Cys Thr Met Gly Pro Gly Lys Val Phe Gly Glu Leu Ala
                    420                    425                    430
     Ile Leu Tyr Asn Cys Thr Arg Thr Ala Thr Val Lys Thr Leu Val Asn
                    435                    440                    445
     Val Lys Leu Trp Ala Ile Asp Arg Gln Cys Phe Gln Thr Ile Met Met
15   450                    455                    460
     Arg Thr Gly Leu Ile Lys His Thr Glu Tyr Met Glu Phe Leu Lys Ser
     465                    470                    475                    480
     Val Pro Thr Phe Gln Ser Leu Pro Glu Glu Ile Leu Ser Lys Leu Ala
                    485                    490                    495
20   Asp Val Leu Glu Glu Thr His Tyr Glu Asn Gly Glu Tyr Ile Ile Arg
                    500                    505                    510
     Gln Gly Ala Arg Gly Asp Thr Phe Phe Ile Ile Ser Lys Gly Thr Val
             515                    520                    525
     Asn Val Thr Arg Glu Asp Ser Pro Ser Glu Asp Pro Val Phe Leu Arg
25   530                    535                    540
     Thr Leu Gly Lys Gly Asp Trp Phe Gly Glu Lys Ala Leu Gln Gly Glu
     545                    550                    555                    560
     Asp Val Arg Thr Ala Asn Val Ile Ala Ala Glu Ala Val Thr Cys Leu
                    565                    570                    575
30   Val Ile Asp Arg Asp Ser Phe Lys His Leu Ile Gly Gly Leu Asp Asp
                    580                    585                    590
     Val Ser Asn Lys Ala Tyr Glu Asp Ala Glu Ala Lys Ala Lys Tyr Glu
             595                    600                    605
     Ala Glu Ala Ala Phe Phe Ala Asn Leu Lys Leu Ser Asp Phe Asn Ile
35   610                    615                    620
     Ile Asp Thr Leu Gly Val Gly Gly Phe Gly Arg Val Glu Leu Val Gln
     625                    630                    635                    640
     Leu Lys Ser Glu Glu Ser Lys Thr Phe Ala Met Lys Ile Leu Lys Lys
                    645                    650                    655
40   Arg His Ile Val Asp Thr Arg Gln Gln Glu His Ile Arg Ser Glu Lys
                    660                    665                    670
     Gln Ile Met Gln Gly Ala His Ser Asp Phe Ile Val Arg Leu Tyr Arg
             675                    680                    685
     Thr Phe Lys Asp Ser Lys Tyr Leu Tyr Met Leu Met Glu Ala Cys Leu
45   690                    695                    700
     Gly Gly Glu Leu Trp Thr Ile Leu Arg Asp Arg Gly Ser Phe Glu Asp
     705                    710                    715                    720
     Ser Thr Thr Arg Phe Tyr Thr Ala Cys Val Val Glu Ala Phe Ala Tyr
                    725                    730                    735
50   Leu His Ser Lys Gly Ile Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu
             740                    745                    750
     Ile Leu Asp His Arg Gly Tyr Ala Lys Leu Val Asp Phe Gly Phe Ala
             755                    760                    765
     Lys Lys Ile Gly Phe Gly Lys Lys Thr Trp Thr Phe Cys Gly Thr Pro
55   770                    775                    780
     Glu Tyr Val Ala Pro Glu Ile Ile Leu Asn Lys Gly His Asp Ile Ser
```

276

```
785                      790                      795                      800
Ala Asp Tyr Trp Ser Leu Gly Ile Leu Met Tyr Glu Leu Leu Thr Gly
                805                      810                      815
Ser Pro Pro Phe Ser Gly Pro Asp Pro Met Lys Thr Tyr Asn Ile Ile
                820                      825                      830
Leu Arg Gly Ile Asp Met Ile Glu Phe Pro Lys Lys Ile Ala Lys Asn
            835                      840                      845
Ala Ala Asn Leu Ile Lys Lys Leu Cys Arg Asp Asn Pro Ser Glu Arg
        850                      855                      860
Leu Gly Asn Leu Lys Asn Gly Val Lys Asp Ile Gln Lys His Lys Trp
865                      870                      875                      880
Phe Glu Gly Phe Asn Trp Glu Gly Leu Arg Lys Gly Thr Leu Thr Pro
                885                      890                      895
Pro Ile Ile Pro Ser Val Ala Ser Pro Thr Asp Thr Ser Asn Phe Asp
            900                      905                      910
Ser Phe Pro Glu Asp Asn Asp Glu Pro Pro Asp Asp Asn Ser Gly
        915                      920                      925
Trp Asp Ile Asp Phe
        930
```

        (2) INFORMATION FOR SEQ ID NO:136:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 2799 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: cDNA
        (ix) FEATURE:

            (A) NAME/KEY: Coding Sequence
            (B) LOCATION: 1...2795
            (D) OTHER INFORMATION:

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:

```
ATG GGC ACC TTG CGG GAT TTA CAG TAC GCG CTC CAG GAG AAG ATC GAG    48
Met Gly Thr Leu Arg Asp Leu Gln Tyr Ala Leu Gln Glu Lys Ile Glu
1               5                   10                  15

GAG CTG AGG CAG CGG GAT GCT CTC ATC GAC GAG CTG GAG CTG GAG TTG    96
Glu Leu Arg Gln Arg Asp Ala Leu Ile Asp Glu Leu Glu Leu Glu Leu
                20                  25                  30

GAT CAG AAG GAC GAA CTG ATC CAG AAG CTG CAG AAC GAG CTG GAC AAG   144
Asp Gln Lys Asp Glu Leu Ile Gln Lys Leu Gln Asn Glu Leu Asp Lys
            35                  40                  45

TAC CGC TCG GTG ATC CGA CCA GCC ACC CAG CAG GCG CAG AAG CAG AGC   192
Tyr Arg Ser Val Ile Arg Pro Ala Thr Gln Gln Ala Gln Lys Gln Ser
        50                  55                  60

GCG AGC ACC TTG CAG GGC GAG CCG CGC ACC AAG CGG CAG GCG ATC TCC   240
Ala Ser Thr Leu Gln Gly Glu Pro Arg Thr Lys Arg Gln Ala Ile Ser
65                  70                  75                  80
```

276

```
GCC GAG CCC ACC GCC TTC GAC ATC CAG GAT CTC AGC CAT GTG ACC CTG      288
Ala Glu Pro Thr Ala Phe Asp Ile Gln Asp Leu Ser His Val Thr Leu
                85                  90                  95

CCC TTC TAC CCC AAG AGC CCA CAG TCC AAG GAT CTT ATA AAG GAA GCT      336
Pro Phe Tyr Pro Lys Ser Pro Gln Ser Lys Asp Leu Ile Lys Glu Ala
               100                 105                 110

ATC CTT GAC AAT GAC TTT ATG AAG AAC TTG GAG CTG TCG CAG ATC CAG      384
Ile Leu Asp Asn Asp Phe Met Lys Asn Leu Glu Leu Ser Gln Ile Gln
           115                 120                 125

GAG ATT GTG GAT TGT ATG TAC CCG GTG GAG TAT GGC AAG GAC AGT TGC      432
Glu Ile Val Asp Cys Met Tyr Pro Val Glu Tyr Gly Lys Asp Ser Cys
       130                 135                 140

ATC ATC AAA GAA GGA GAC GTG GGG TCA CTG GTG TAT GTC ATG GAA GAT      480
Ile Ile Lys Glu Gly Asp Val Gly Ser Leu Val Tyr Val Met Glu Asp
145                 150                 155                 160

GGT AAG GTT GAA GTT ACA AAA GAA GGT GTG AAG TTG TGT ACC ATG GGT      528
Gly Lys Val Glu Val Thr Lys Glu Gly Val Lys Leu Cys Thr Met Gly
               165                 170                 175

CCA GGA AAA GTG TTT GGG GAA TTG GCT ATT CTT TAC AAC TGT ACC CGG      576
Pro Gly Lys Val Phe Gly Glu Leu Ala Ile Leu Tyr Asn Cys Thr Arg
               180                 185                 190

ACA GCG ACC GTC AAG ACT CTT GTA AAT GTA AAA CTC TGG GCC ATT GAT      624
Thr Ala Thr Val Lys Thr Leu Val Asn Val Lys Leu Trp Ala Ile Asp
           195                 200                 205

CGA CAA TGT TTT CAA ACA ATA ATG ATG AGG ACA GGA CTC ATC AAG CAT      672
Arg Gln Cys Phe Gln Thr Ile Met Met Arg Thr Gly Leu Ile Lys His
       210                 215                 220

ACC GAG TAT ATG GAA TTT TTA AAA AGC GTT CCA ACA TTC CAG AGC CTT      720
Thr Glu Tyr Met Glu Phe Leu Lys Ser Val Pro Thr Phe Gln Ser Leu
225                 230                 235                 240

CCT GAA GAG ATC CTC AGC AAG CTT GCT GAT GTC CTT GAA GAG ACC CAC      768
Pro Glu Glu Ile Leu Ser Lys Leu Ala Asp Val Leu Glu Glu Thr His
               245                 250                 255

TAT GAA AAT GGA GAA TAT ATT ATC AGG CAA GGT GCA AGA GGG GAC ACC      816
Tyr Glu Asn Gly Glu Tyr Ile Ile Arg Gln Gly Ala Arg Gly Asp Thr
               260                 265                 270

TTC TTT ATC ATC AGC AAA GGA ACG GTA AAT GTC ACT CGT GAA GAC TCA      864
Phe Phe Ile Ile Ser Lys Gly Thr Val Asn Val Thr Arg Glu Asp Ser
           275                 280                 285

CCG AGT GAA GAC CCA GTC TTT CTT AGA ACT TTA GGA AAA GGA GAC TGG      912
Pro Ser Glu Asp Pro Val Phe Leu Arg Thr Leu Gly Lys Gly Asp Trp
           290                 295                 300
```

277

278

```
        TTT GGA GAG AAA GCC TTG CAG GGG GAA GAT GTG AGA ACA GCA AAC GTA        960
        Phe Gly Glu Lys Ala Leu Gln Gly Glu Asp Val Arg Thr Ala Asn Val
        305             310             315             320
5

        ATT GCT GCA GAA GCT GTA ACC TGC CTT GTG ATT GAC AGA GAC TCT TTT        1008
        Ile Ala Ala Glu Ala Val Thr Cys Leu Val Ile Asp Arg Asp Ser Phe
                        325             330             335

10      AAA CAT TTG ATT GGA GGG CTG GAT GAT GTT TCT AAT AAA GCA TAT GAA        1056
        Lys His Leu Ile Gly Gly Leu Asp Asp Val Ser Asn Lys Ala Tyr Glu
                        340             345             350

        GAT GCA GAA GCT AAA GCA AAA TAT GAA GCT GAA GCG GCT TTC TTC GCC        1104
15      Asp Ala Glu Ala Lys Ala Lys Tyr Glu Ala Glu Ala Ala Phe Phe Ala
                355             360             365

        AAC CTG AAG CTG TCT GAT TTC AAC ATC ATT GAT ACC CTT GGA GTT GGA        1152
        Asn Leu Lys Leu Ser Asp Phe Asn Ile Ile Asp Thr Leu Gly Val Gly
20          370             375             380

        GGT TTC GGA CGA GTA GAA CTG GTC CAG TTG AAA AGT GAA GAA TCC AAA        1200
        Gly Phe Gly Arg Val Glu Leu Val Gln Leu Lys Ser Glu Glu Ser Lys
        385             390             395             400
25

        ACG TTT GCA ATG AAG ATT CTC AAG AAA CGT CAC ATT GTG GAC ACA AGA        1248
        Thr Phe Ala Met Lys Ile Leu Lys Lys Arg His Ile Val Asp Thr Arg
                        405             410             415

30      CAG CAG GAG CAC ATC CGC TCA GAG AAG CAG ATC ATG CAG GGG GCT CAT        1296
        Gln Gln Glu His Ile Arg Ser Glu Lys Gln Ile Met Gln Gly Ala His
                        420             425             430

        TCC GAT TTC ATA GTG AGA CTG TAC AGA ACA TTT AAG GAC AGC AAA TAT        1344
35      Ser Asp Phe Ile Val Arg Leu Tyr Arg Thr Phe Lys Asp Ser Lys Tyr
                435             440             445

        TTG TAT ATG TTG ATG GAA GCT TGT CTA GGT GGA GAG CTC TGG ACC ATT        1392
        Leu Tyr Met Leu Met Glu Ala Cys Leu Gly Gly Glu Leu Trp Thr Ile
40          450             455             460

        CTC AGG GAT AGA GGT TCG TTT GAA GAT TCT ACA ACC AGA TTT TAC ACA        1440
        Leu Arg Asp Arg Gly Ser Phe Glu Asp Ser Thr Thr Arg Phe Tyr Thr
        465             470             475             480
45

        GCA TGT GTG GTA GAA GCT TTT GCC TAT CTG CAT TCC AAA GGA ATC ATT        1488
        Ala Cys Val Val Glu Ala Phe Ala Tyr Leu His Ser Lys Gly Ile Ile
                        485             490             495

50      TAC AGG GAC CTC AAG CCA GAA AAT CTC ATC CTA GAT CAC CGA GGT TAT        1536
        Tyr Arg Asp Leu Lys Pro Glu Asn Leu Ile Leu Asp His Arg Gly Tyr
                        500             505             510

        GCC AAA CTG GTT GAT TTT GGC TTT GCA AAG AAA ATA GGA TTT GGA AAG        1584
55      Ala Lys Leu Val Asp Phe Gly Phe Ala Lys Lys Ile Gly Phe Gly Lys
                515             520             525
```

SUBSTITUTE SHEET (RULE 26)

```
     AAA ACA TGG ACT TTT TGT GGG ACT CCA GAG TAT GTA GCC CCA GAG ATC   1632
     Lys Thr Trp Thr Phe Cys Gly Thr Pro Glu Tyr Val Ala Pro Glu Ile
         530             535                 540
 5
     ATC CTG AAC AAA GGC CAT GAC ATT TCA GCC GAC TAC TGG TCA CTG GGA   1680
     Ile Leu Asn Lys Gly His Asp Ile Ser Ala Asp Tyr Trp Ser Leu Gly
     545             550                 555                 560

10   ATC CTA ATG TAT GAA CTC CTG ACT GGC AGC CCA CCT TTC TCA GGC CCA   1728
     Ile Leu Met Tyr Glu Leu Leu Thr Gly Ser Pro Pro Phe Ser Gly Pro
                     565                 570                 575

     GAT CCT ATG AAA ACC TAT AAC ATC ATA TTG AGG GGG ATT GAC ATG ATA   1776
15   Asp Pro Met Lys Thr Tyr Asn Ile Ile Leu Arg Gly Ile Asp Met Ile
                 580                 585                 590

     GAA TTT CCA AAG AAG ATT GCC AAA AAT GCT GCT AAT TTA ATT AAA AAA   1824
     Glu Phe Pro Lys Lys Ile Ala Lys Asn Ala Ala Asn Leu Ile Lys Lys
20           595                 600                 605

     CTA TGC AGG GAC AAT CCA TCA GAA AGA TTA GGG AAT TTG AAA AAT GGA   1872
     Leu Cys Arg Asp Asn Pro Ser Glu Arg Leu Gly Asn Leu Lys Asn Gly
         610                 615                 620
25
     GTA AAA GAC ATT CAA AAG CAC AAA TGG TTT GAG GGC TTT AAC TGG GAA   1920
     Val Lys Asp Ile Gln Lys His Lys Trp Phe Glu Gly Phe Asn Trp Glu
     625             630                 635                 640

30   GGC TTA AGA AAA GGT ACC TTG ACA CCT CCT ATA ATA CCA AGT GTT GCA   1968
     Gly Leu Arg Lys Gly Thr Leu Thr Pro Pro Ile Ile Pro Ser Val Ala
                     645                 650                 655

     TCA CCC ACA GAC ACA AGT AAT TTT GAC AGT TTC CCT GAG GAC AAC GAT   2016
35   Ser Pro Thr Asp Thr Ser Asn Phe Asp Ser Phe Pro Glu Asp Asn Asp
                 660                 665                 670

     GAA CCA CCA CCT GAT GAC AAC TCA GGA TGG GAT ATA GAC TTC TCG GAT   2064
     Glu Pro Pro Pro Asp Asp Asn Ser Gly Trp Asp Ile Asp Phe Ser Asp
40           675                 680                 685

     CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG   2112
     Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
             690                 695                 700
45
     GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG   2160
     Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
     705                 710                 715                 720

50   TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG   2208
     Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
                     725                 730                 735

     ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC   2256
55   Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
                 740                 745                 750
```

279

```
ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC    2304
Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
        755                 760                 765
```

```
CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA    2352
Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
        770                 775                 780
```

```
GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC    2400
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
785                 790                 795                 800
```

```
AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC    2448
Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
                805                 810                 815
```

```
ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG    2496
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
                820                 825                 830
```

```
CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC    2544
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
        835                 840                 845
```

```
GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC    2592
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
        850                 855                 860
```

```
ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC    2640
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
865                 870                 875                 880
```

```
CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC    2688
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
                885                 890                 895
```

```
ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG    2736
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
                900                 905                 910
```

```
GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC    2784
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
                915                 920                 925
```

```
GAG CTG TAC AA GTAA                                                2799
Glu Leu Tyr Lys
        930
```

(2) INFORMATION FOR SEQ ID NO:137:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 932 amino acids
        (B) TYPE: amino acid
        (C) STRANDEDNESS: single

SUBSTITUTE SHEET (RULE 26)

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

```
Met Gly Thr Leu Arg Asp Leu Gln Tyr Ala Leu Gln Glu Lys Ile Glu
 1               5                  10                  15
Glu Leu Arg Gln Arg Asp Ala Leu Ile Asp Glu Leu Glu Leu Glu Leu
            20                  25                  30
Asp Gln Lys Asp Glu Leu Ile Gln Lys Leu Gln Asn Glu Leu Asp Lys
            35                  40                  45
Tyr Arg Ser Val Ile Arg Pro Ala Thr Gln Gln Ala Gln Lys Gln Ser
    50                  55                  60
Ala Ser Thr Leu Gln Gly Glu Pro Arg Thr Lys Arg Gln Ala Ile Ser
65                  70                  75                  80
Ala Glu Pro Thr Ala Phe Asp Ile Gln Asp Leu Ser His Val Thr Leu
                85                  90                  95
Pro Phe Tyr Pro Lys Ser Pro Gln Ser Lys Asp Leu Ile Lys Glu Ala
            100                 105                 110
Ile Leu Asp Asn Asp Phe Met Lys Asn Leu Glu Leu Ser Gln Ile Gln
            115                 120                 125
Glu Ile Val Asp Cys Met Tyr Pro Val Glu Tyr Gly Lys Asp Ser Cys
    130                 135                 140
Ile Ile Lys Glu Gly Asp Val Gly Ser Leu Val Tyr Val Met Glu Asp
145                 150                 155                 160
Gly Lys Val Glu Val Thr Lys Glu Gly Val Lys Leu Cys Thr Met Gly
                165                 170                 175
Pro Gly Lys Val Phe Gly Glu Leu Ala Ile Leu Tyr Asn Cys Thr Arg
            180                 185                 190
Thr Ala Thr Val Lys Thr Leu Val Asn Val Lys Leu Trp Ala Ile Asp
            195                 200                 205
Arg Gln Cys Phe Gln Thr Ile Met Met Arg Thr Gly Leu Ile Lys His
    210                 215                 220
Thr Glu Tyr Met Glu Phe Leu Lys Ser Val Pro Thr Phe Gln Ser Leu
225                 230                 235                 240
Pro Glu Glu Ile Leu Ser Lys Leu Ala Asp Val Leu Glu Glu Thr His
                245                 250                 255
Tyr Glu Asn Gly Glu Tyr Ile Ile Arg Gln Gly Ala Arg Gly Asp Thr
                260                 265                 270
Phe Phe Ile Ile Ser Lys Gly Thr Val Asn Val Thr Arg Glu Asp Ser
            275                 280                 285
Pro Ser Glu Asp Pro Val Phe Leu Arg Thr Leu Gly Lys Gly Asp Trp
            290                 295                 300
Phe Gly Glu Lys Ala Leu Gln Gly Glu Asp Val Arg Thr Ala Asn Val
305                 310                 315                 320
Ile Ala Ala Glu Ala Val Thr Cys Leu Val Ile Asp Arg Asp Ser Phe
                325                 330                 335
Lys His Leu Ile Gly Gly Leu Asp Asp Val Ser Asn Lys Ala Tyr Glu
                340                 345                 350
Asp Ala Glu Ala Lys Ala Lys Tyr Glu Ala Glu Ala Ala Phe Phe Ala
            355                 360                 365
Asn Leu Lys Leu Ser Asp Phe Asn Ile Ile Asp Thr Leu Gly Val Gly
            370                 375                 380
Gly Phe Gly Arg Val Glu Leu Val Gln Leu Lys Ser Glu Glu Ser Lys
```

BNSDOCID: <WO___9845704A2_I_>

```
         385                      390                      395                      400
         Thr Phe Ala Met Lys Ile Leu Lys Lys Arg His Ile Val Asp Thr Arg
                         405                      410                      415
         Gln Gln Glu His Ile Arg Ser Glu Lys Gln Ile Met Gln Gly Ala His
  5                      420                      425                      430
         Ser Asp Phe Ile Val Arg Leu Tyr Arg Thr Phe Lys Asp Ser Lys Tyr
                         435                      440                      445
         Leu Tyr Met Leu Met Glu Ala Cys Leu Gly Gly Glu Leu Trp Thr Ile
                         450                      455                      460
 10      Leu Arg Asp Arg Gly Ser Phe Glu Asp Ser Thr Thr Arg Phe Tyr Thr
         465                      470                      475                      480
         Ala Cys Val Val Glu Ala Phe Ala Tyr Leu His Ser Lys Gly Ile Ile
                         485                      490                      495
         Tyr Arg Asp Leu Lys Pro Glu Asn Leu Ile Leu Asp His Arg Gly Tyr
 15                      500                      505                      510
         Ala Lys Leu Val Asp Phe Gly Phe Ala Lys Lys Ile Gly Phe Gly Lys
                         515                      520                      525
         Lys Thr Trp Thr Phe Cys Gly Thr Pro Glu Tyr Val Ala Pro Glu Ile
                         530                      535                      540
 20      Ile Leu Asn Lys Gly His Asp Ile Ser Ala Asp Tyr Trp Ser Leu Gly
         545                      550                      555                      560
         Ile Leu Met Tyr Glu Leu Leu Thr Gly Ser Pro Pro Phe Ser Gly Pro
                         565                      570                      575
         Asp Pro Met Lys Thr Tyr Asn Ile Ile Leu Arg Gly Ile Asp Met Ile
 25                      580                      585                      590
         Glu Phe Pro Lys Lys Ile Ala Lys Asn Ala Ala Asn Leu Ile Lys Lys
                         595                      600                      605
         Leu Cys Arg Asp Asn Pro Ser Glu Arg Leu Gly Asn Leu Lys Asn Gly
                         610                      615                      620
 30      Val Lys Asp Ile Gln Lys His Lys Trp Phe Glu Gly Phe Asn Trp Glu
         625                      630                      635                      640
         Gly Leu Arg Lys Gly Thr Leu Thr Pro Pro Ile Ile Pro Ser Val Ala
                         645                      650                      655
         Ser Pro Thr Asp Thr Ser Asn Phe Asp Ser Phe Pro Glu Asp Asn Asp
 35                      660                      665                      670
         Glu Pro Pro Pro Asp Asp Asn Ser Gly Trp Asp Ile Asp Phe Ser Asp
                         675                      680                      685
         Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
                         690                      695                      700
 40      Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
         705                      710                      715                      720
         Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
                         725                      730                      735
         Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
 45                      740                      745                      750
         Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
                         755                      760                      765
         Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
                         770                      775                      780
 50      Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
         785                      790                      795                      800
         Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
                         805                      810                      815
         Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
 55                      820                      825                      830
         His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
```

```
           835                    840                    845
     Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
        850                    855                    860
     Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
 5      865                    870                    875                    880
     Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
                           885                    890                    895
     Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
                           900                    905                    910
10   Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
                           915                    920                    925
     Glu Leu Tyr Lys
        930
```

15   (2) INFORMATION FOR SEQ ID NO:138:

            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 2184 base pairs
                (B) TYPE: nucleic acid
20   (C) STRANDEDNESS: single
                (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: cDNA
            (ix) FEATURE:
25
                (A) NAME/KEY: Coding Sequence
                (B) LOCATION: 1...2181
                (D) OTHER INFORMATION:

30   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:

```
     ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5                  10                  15
35
     GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                  20                  25                  30

40   GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
     Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                  35                  40                  45

     TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
45   Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                  50                  55                  60

     CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
50    65                  70                  75                  80

     CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                       85                  90                  95
55
     CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
```

BNSDOCID: <WO___9845704A2_I_>

284

```
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                 100                     105                 110

     GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC    384
  5  Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
                 115                     120                 125

     ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC    432
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 10              130                     135                 140

     AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC    480
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
     145                     150                     155             160
 15
     GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC    528
     Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                     165                     170                 175

 20  GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC    576
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                     180                     185                 190

     CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG    624
 25  Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
                     195                     200                 205

     AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
 30      210                     215                     220

     GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                     230                     235                 240
 35
     GGA CTC AGA TCT CGA GGC ACC ATG AGC GAC GTG GCT ATT GTG AAG GAG    768
     Gly Leu Arg Ser Arg Gly Thr Met Ser Asp Val Ala Ile Val Lys Glu
                     245                     250                 255

 40  GGT TGG CTG CAC AAA CGA GGG GAG TAC ATC AAG ACC TGG CGG CCA CGC    816
     Gly Trp Leu His Lys Arg Gly Glu Tyr Ile Lys Thr Trp Arg Pro Arg
                     260                     265                 270

     TAC TTC CTC CTC AAG AAT GAT GGC ACC TTC ATT GGC TAC AAG GAG CGG    864
 45  Tyr Phe Leu Leu Lys Asn Asp Gly Thr Phe Ile Gly Tyr Lys Glu Arg
                     275                     280                 285

     CCG CAG GAT GTG GAC CAA CGT GAG GCT CCC CTC AAC AAC TTC TCT GTG    912
     Pro Gln Asp Val Asp Gln Arg Glu Ala Pro Leu Asn Asn Phe Ser Val
 50      290                     295                     300

     GCG CAG TGC CAG CTG ATG AAG ACG GAG CGG CCC CGG CCC AAC ACC TTC    960
     Ala Gln Cys Gln Leu Met Lys Thr Glu Arg Pro Arg Pro Asn Thr Phe
     305                     310                     315             320
 55
     ATC ATC CGC TGC CTG CAG TGG ACC ACT GTC ATC GAA CGC ACC TTC CAT   1008
```

284

SUBSTITUTE SHEET (RULE 26)

```
        Ile Ile Arg Cys Leu Gln Trp Thr Thr Val Ile Glu Arg Thr Phe His
                325                 330                 335

     5  GTG GAG ACT CCT GAG GAG CGG GAG GAG TGG ACA ACC GCC ATC CAG ACT      1056
        Val Glu Thr Pro Glu Glu Arg Glu Glu Trp Thr Thr Ala Ile Gln Thr
                    340                 345                 350

        GTG GCT GAC GGC CTC AAG AAG CAG GAG GAG GAG GAG ATG GAC TTC CGG      1104
        Val Ala Asp Gly Leu Lys Lys Gln Glu Glu Glu Glu Met Asp Phe Arg
    10              355                 360                 365

        TCG GGC TCA CCC AGT GAC AAC TCA GGG GCT GAA GAG ATG GAG GTG TCC      1152
        Ser Gly Ser Pro Ser Asp Asn Ser Gly Ala Glu Glu Met Glu Val Ser
                370                 375                 380
    15
        CTG GCC AAG CCC AAG CAC CGC GTG ACC ATG AAC GAG TTT GAG TAC CTG      1200
        Leu Ala Lys Pro Lys His Arg Val Thr Met Asn Glu Phe Glu Tyr Leu
        385                 390                 395                 400

    20  AAG CTG CTG GGC AAG GGC ACT TTC GGC AAG GTG ATC CTG GTG AAG GAG      1248
        Lys Leu Leu Gly Lys Gly Thr Phe Gly Lys Val Ile Leu Val Lys Glu
                        405                 410                 415

        AAG GCC ACA GGC CGC TAC TAC GCC ATG AAG ATC CTC AAG AAG GAA GTC      1296
    25  Lys Ala Thr Gly Arg Tyr Tyr Ala Met Lys Ile Leu Lys Lys Glu Val
                    420                 425                 430

        ATC GTG GCC AAG GAC GAG GTG GCC CAC ACA CTC ACC GAG AAC CGC GTC      1344
        Ile Val Ala Lys Asp Glu Val Ala His Thr Leu Thr Glu Asn Arg Val
    30              435                 440                 445

        CTG CAG AAC TCC AGG CAC CCC TTC CTC ACA GCC CTG AAG TAC TCT TTC      1392
        Leu Gln Asn Ser Arg His Pro Phe Leu Thr Ala Leu Lys Tyr Ser Phe
                450                 455                 460
    35
        CAG ACC CAC GAC CGC CTC TGC TTT GTC ATG GAG TAC GCC AAC GGG GGC      1440
        Gln Thr His Asp Arg Leu Cys Phe Val Met Glu Tyr Ala Asn Gly Gly
        465                 470                 475                 480

    40  GAG CTG TTC TTC CAC CTG TCC CGG GAA CGT GTG TTC TCC GAG GAC CGG      1488
        Glu Leu Phe Phe His Leu Ser Arg Glu Arg Val Phe Ser Glu Asp Arg
                        485                 490                 495

        GCC CGC TTC TAT GGC GCT GAG ATT GTG TCA GCC CTG GAC TAC CTG CAC      1536
    45  Ala Arg Phe Tyr Gly Ala Glu Ile Val Ser Ala Leu Asp Tyr Leu His
                    500                 505                 510

        TCG GAG AAG AAC GTG GTG TAC CGG GAC CTC AAG CTG GAG AAC CTC ATG      1584
        Ser Glu Lys Asn Val Val Tyr Arg Asp Leu Lys Leu Glu Asn Leu Met
    50              515                 520                 525

        CTG GAC AAG GAC GGG CAC ATT AAG ATC ACA GAC TTC GGG CTG TGC AAG      1632
        Leu Asp Lys Asp Gly His Ile Lys Ile Thr Asp Phe Gly Leu Cys Lys
                530                 535                 540
    55
        GAG GGG ATC AAG GAC GGT GCC ACC ATG AAG ACC TTT TGC GGC ACA CCT      1680
```

285

286

```
            Glu Gly Ile Lys Asp Gly Ala Thr Met Lys Thr Phe Cys Gly Thr Pro
            545             550             555             560

  5         GAG TAC CTG GCC CCC GAG GTG CTG GAG GAC AAT GAC TAC GGC CGT GCA      1728
            Glu Tyr Leu Ala Pro Glu Val Leu Glu Asp Asn Asp Tyr Gly Arg Ala
                        565             570             575

            GTG GAC TGG TGG GGG CTG GGC GTG GTC ATG TAC GAG ATG ATG TGC GGT      1776
            Val Asp Trp Trp Gly Leu Gly Val Val Met Tyr Glu Met Met Cys Gly
 10                 580             585             590

            CGC CTG CCC TTC TAC AAC CAG GAC CAT GAG AAG CTT TTT GAG CTC ATC      1824
            Arg Leu Pro Phe Tyr Asn Gln Asp His Glu Lys Leu Phe Glu Leu Ile
                    595             600             605
 15
            CTC ATG GAG GAG ATC CGC TTC CCG CGC ACG CTT GGT CCC GAG GCC AAG      1872
            Leu Met Glu Glu Ile Arg Phe Pro Arg Thr Leu Gly Pro Glu Ala Lys
                610             615             620

 20         TCC TTG CTT TCA GGG CTG CTC AAG AAG GAC CCC AAG CAG AGG CTT GGC      1920
            Ser Leu Leu Ser Gly Leu Leu Lys Lys Asp Pro Lys Gln Arg Leu Gly
            625             630             635             640

            GGG GGC TCC GAG GAC GCC AAG GAG ATC ATG CAG CAT CGC TTC TTT GCC      1968
 25         Gly Gly Ser Glu Asp Ala Lys Glu Ile Met Gln His Arg Phe Phe Ala
                        645             650             655

            GGT ATC GTG TGG CAG CAC GTG TAC GAG AAG AAG CTC AGC CCA CCC TTC      2016
            Gly Ile Val Trp Gln His Val Tyr Glu Lys Lys Leu Ser Pro Pro Phe
 30                 660             665             670

            AAG CCC CAG GTC ACG TCG GAG ACT GAC ACC AGG TAT TTT GAT GAG GAG      2064
            Lys Pro Gln Val Thr Ser Glu Thr Asp Thr Arg Tyr Phe Asp Glu Glu
                    675             680             685
 35
            TTC ACG GCC CAG ATG ATC ACC ATC ACA CCA CCT GAC CAA GAT GAC AGC      2112
            Phe Thr Ala Gln Met Ile Thr Ile Thr Pro Pro Asp Gln Asp Asp Ser
                690             695             700

 40         ATG GAG TGT GTG GAC AGC GAG CGC AGG CCC CAC TTC CCC CAG TTC TCC      2160
            Met Glu Cys Val Asp Ser Glu Arg Arg Pro His Phe Pro Gln Phe Ser
            705             710             715             720

            TAC TCG GCC AGC AGC ACG GCC TGA                                     2184
 45         Tyr Ser Ala Ser Ser Thr Ala
                        725
```

            (2) INFORMATION FOR SEQ ID NO:139:
 50
            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 727 amino acids
                (B) TYPE: amino acid
                (C) STRANDEDNESS: single
 55   (D) TOPOLOGY: linear

SUBSTITUTE SHEET (RULE 26)

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1               5                   10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
            35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
        50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
        130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
            195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
            210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Gly Thr Met Ser Asp Val Ala Ile Val Lys Glu
                245                 250                 255
Gly Trp Leu His Lys Arg Gly Glu Tyr Ile Lys Thr Trp Arg Pro Arg
                260                 265                 270
Tyr Phe Leu Leu Lys Asn Asp Gly Thr Phe Ile Gly Tyr Lys Glu Arg
            275                 280                 285
Pro Gln Asp Val Asp Gln Arg Glu Ala Pro Leu Asn Asn Phe Ser Val
            290                 295                 300
Ala Gln Cys Gln Leu Met Lys Thr Glu Arg Pro Arg Pro Asn Thr Phe
305                 310                 315                 320
Ile Ile Arg Cys Leu Gln Trp Thr Thr Val Ile Glu Arg Thr Phe His
                325                 330                 335
Val Glu Thr Pro Glu Glu Arg Glu Glu Trp Thr Thr Ala Ile Gln Thr
            340                 345                 350
Val Ala Asp Gly Leu Lys Lys Gln Glu Glu Glu Met Asp Phe Arg
            355                 360                 365
Ser Gly Ser Pro Ser Asp Asn Ser Gly Ala Glu Glu Met Glu Val Ser
            370                 375                 380
Leu Ala Lys Pro Lys His Arg Val Thr Met Asn Glu Phe Glu Tyr Leu
385                 390                 395                 400
Lys Leu Leu Gly Lys Gly Thr Phe Gly Lys Val Ile Leu Val Lys Glu
```

			405				410					415	

```
                           405                     410                     415
      Lys Ala Thr Gly Arg Tyr Tyr Ala Met Lys Ile Leu Lys Lys Glu Val
                    420                     425                     430
      Ile Val Ala Lys Asp Glu Val Ala His Thr Leu Thr Glu Asn Arg Val
 5                435                     440                     445
      Leu Gln Asn Ser Arg His Pro Phe Leu Thr Ala Leu Lys Tyr Ser Phe
               450                     455                     460
      Gln Thr His Asp Arg Leu Cys Phe Val Met Glu Tyr Ala Asn Gly Gly
      465                     470                     475                     480
10    Glu Leu Phe Phe His Leu Ser Arg Glu Arg Val Phe Ser Glu Asp Arg
                        485                     490                     495
      Ala Arg Phe Tyr Gly Ala Glu Ile Val Ser Ala Leu Asp Tyr Leu His
                    500                     505                     510
      Ser Glu Lys Asn Val Val Tyr Arg Asp Leu Lys Leu Glu Asn Leu Met
15             515                     520                     525
      Leu Asp Lys Asp Gly His Ile Lys Ile Thr Asp Phe Gly Leu Cys Lys
               530                     535                     540
      Glu Gly Ile Lys Asp Gly Ala Thr Met Lys Thr Phe Cys Gly Thr Pro
      545                     550                     555                     560
20    Glu Tyr Leu Ala Pro Glu Val Leu Glu Asp Asn Asp Tyr Gly Arg Ala
                        565                     570                     575
      Val Asp Trp Trp Gly Leu Gly Val Val Met Tyr Glu Met Met Cys Gly
                    580                     585                     590
      Arg Leu Pro Phe Tyr Asn Gln Asp His Glu Lys Leu Phe Glu Leu Ile
25             595                     600                     605
      Leu Met Glu Glu Ile Arg Phe Pro Arg Thr Leu Gly Pro Glu Ala Lys
               610                     615                     620
      Ser Leu Leu Ser Gly Leu Leu Lys Lys Asp Pro Lys Gln Arg Leu Gly
      625                     630                     635                     640
30    Gly Gly Ser Glu Asp Ala Lys Glu Ile Met Gln His Arg Phe Phe Ala
                        645                     650                     655
      Gly Ile Val Trp Gln His Val Tyr Glu Lys Lys Leu Ser Pro Pro Phe
                    660                     665                     670
      Lys Pro Gln Val Thr Ser Glu Thr Asp Thr Arg Tyr Phe Asp Glu Glu
35             675                     680                     685
      Phe Thr Ala Gln Met Ile Thr Ile Thr Pro Pro Asp Gln Asp Asp Ser
               690                     695                     700
      Met Glu Cys Val Asp Ser Glu Arg Arg Pro His Phe Pro Gln Phe Ser
      705                     710                     715                     720
40    Tyr Ser Ala Ser Ser Thr Ala
                    725
```

                    (2) INFORMATION FOR SEQ ID NO:140:

45   (i) SEQUENCE CHARACTERISTICS:
                        (A) LENGTH: 2394 base pairs
                        (B) TYPE: nucleic acid
                        (C) STRANDEDNESS: single
                        (D) TOPOLOGY: linear
50
                    (ii) MOLECULE TYPE: cDNA
                    (ix) FEATURE:

                        (A) NAME/KEY: Coding Sequence
55   (B) LOCATION: 1...2391
                        (D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

```
        ATG GAC GAA CTG TTC CCC CTC ATC TTC CCG GCA GAG CCA GCC CAG GCC    48
 5      Met Asp Glu Leu Phe Pro Leu Ile Phe Pro Ala Glu Pro Ala Gln Ala
         1               5                  10                  15

        TCT GGC CCC TAT GTG GAG ATC ATT GAG CAG CCC AAG CAG CGG GGC ATG    96
        Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln Pro Lys Gln Arg Gly Met
 10                      20                  25                  30

        CGC TTC CGC TAC AAG TGC GAG GGG CGC TCC GCG GGC AGC ATC CCA GGC   144
        Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser Ala Gly Ser Ile Pro Gly
                    35                  40                  45
 15
        GAG AGG AGC ACA GAT ACC ACC AAG ACC CAC CCC ACC ATC AAG ATC AAT   192
        Glu Arg Ser Thr Asp Thr Thr Lys Thr His Pro Thr Ile Lys Ile Asn
             50                  55                  60

 20     GGC TAC ACA GGA CCA GGG ACA GTG CGC ATC TCC CTG GTC ACC AAG GAC   240
        Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile Ser Leu Val Thr Lys Asp
        65                  70                  75                  80

        CCT CCT CAC CGG CCT CAC CCC CAC GAG CTT GTA GGA AAG GAC TGC CGG   288
 25     Pro Pro His Arg Pro His Pro His Glu Leu Val Gly Lys Asp Cys Arg
                        85                  90                  95

        GAT GGC TTC TAT GAG GCT GAG CTC TGC CCG GAC CGC TGC ATC CAC AGT   336
        Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro Asp Arg Cys Ile His Ser
 30                     100                 105                 110

        TTC CAG AAC CTG GGA ATC CAG TGT GTG AAG AAG CGG GAC CTG GAG CAG   384
        Phe Gln Asn Leu Gly Ile Gln Cys Val Lys Lys Arg Asp Leu Glu Gln
                    115                 120                 125
 35
        GCT ATC AGT CAG CGC ATC CAG ACC AAC AAC AAC CCC TTC CAA GTT CCT   432
        Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn Asn Pro Phe Gln Val Pro
                 130                 135                 140

 40     ATA GAA GAG CAG CGT GGG GAC TAC GAC CTG AAT GCT GTG CGG CTC TGC   480
        Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu Asn Ala Val Arg Leu Cys
        145                 150                 155                 160

        TTC CAG GTG ACA GTG CGG GAC CCA TCA GGC AGG CCC CTC CGC CTG CCG   528
 45     Phe Gln Val Thr Val Arg Asp Pro Ser Gly Arg Pro Leu Arg Leu Pro
                        165                 170                 175

        CCT GTC CTT CCT CAT CCC ATC TTT GAC AAT CGT GCC CCC AAC ACT GCC   576
        Pro Val Leu Pro His Pro Ile Phe Asp Asn Arg Ala Pro Asn Thr Ala
 50                     180                 185                 190

        GAG CTC AAG ATC TGC CGA GTG AAC CGA AAC TCT GGC AGC TGC CTC GGT   624
        Glu Leu Lys Ile Cys Arg Val Asn Arg Asn Ser Gly Ser Cys Leu Gly
                    195                 200                 205
 55
        GGG GAT GAG ATC TTC CTA CTG TGT GAC AAG GTG CAG AAA GAG GAC ATT   672
```

290

```
        Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys Val Gln Lys Glu Asp Ile
        210                     215              .      220

   5    GAG GTG TAT TTC ACG GGA CCA GGC TGG GAG GCC CGA GGC TCC TTT TCG        720
        Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu Ala Arg Gly Ser Phe Ser
        225                     230              235              240

        CAA GCT GAT GTG CAC CGA CAA GTG GCC ATT GTG TTC CGG ACC CCT CCC        768
  10    Gln Ala Asp Val His Arg Gln Val Ala Ile Val Phe Arg Thr Pro Pro
                            245              250              255

        TAC GCA GAC CCC AGC CTG CAG GCT CCT GTG CGT GTC TCC ATG CAG CTG        816
        Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val Arg Val Ser Met Gln Leu
                        260              265              270
  15
        CGG CGG CCT TCC GAC CGG GAG CTC AGT GAG CCC ATG GAA TTC CAG TAC        864
        Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu Pro Met Glu Phe Gln Tyr
                        275              280              285

  20    CTG CCA GAT ACA GAC GAT CGT CAC CGG ATT GAG GAG AAA CGT AAA AGG        912
        Leu Pro Asp Thr Asp Asp Arg His Arg Ile Glu Glu Lys Arg Lys Arg
                        290              295              300

        ACA TAT GAG ACC TTC AAG AGC ATC ATG AAG AAG AGT CCT TTC AGC GGA        960
  25    Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys Lys Ser Pro Phe Ser Gly
        305                     310              315              320

        CCC ACC GAC CCC CGG CCT CCA CCT CGA CGC ATT GCT GTG CCT TCC CGC       1008
        Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg Ile Ala Val Pro Ser Arg
  30                        325              330              335

        AGC TCA GCT TCT GTC CCC AAG CCA GCA CCC CAG CCC TAT CCC TTT ACG       1056
        Ser Ser Ala Ser Val Pro Lys Pro Ala Pro Gln Pro Tyr Pro Phe Thr
                        340              345              350
  35
        TCA TCC CTG AGC ACC ATC AAC TAT GAT GAG TTT CCC ACC ATG GTG TTT       1104
        Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu Phe Pro Thr Met Val Phe
                        355              360              365

  40    CCT TCT GGG CAG ATC AGC CAG GCC TCG GCC TTG GCC CCG GCC CCT CCC       1152
        Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala Leu Ala Pro Ala Pro Pro
                        370              375              380

        CAA GTC CTG CCC CAG GCT CCA GCC CCT GCC CCT GCT CCA GCC ATG GTA       1200
  45    Gln Val Leu Pro Gln Ala Pro Ala Pro Ala Pro Ala Pro Ala Met Val
        385                     390              395              400

        TCA GCT CTG GCC CAG GCC CCA GCC CCT GTC CCA GTC CTA GCC CCA GGC       1248
        Ser Ala Leu Ala Gln Ala Pro Ala Pro Val Pro Val Leu Ala Pro Gly
                        405              410              415
  50
        CCT CCT CAG GCT GTG GCC CCA CCT GCC CCC AAG CCC ACC CAG GCT GGG       1296
        Pro Pro Gln Ala Val Ala Pro Pro Ala Pro Lys Pro Thr Gln Ala Gly
                        420              425              430
  55
        GAA GGA ACG CTG TCA GAG GCC CTG CTG CAG CTG CAG TTT GAT GAT GAA       1344
```

290

```
          Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln Leu Gln Phe Asp Asp Glu
                  435             440             445

   5      GAC CTG GGG GCC TTG CTT GGC AAC AGC ACA GAC CCA GCT GTG TTC ACA   1392
          Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr Asp Pro Ala Val Phe Thr
                  450             455             460

  10      GAC CTG GCA TCC GTC GAC AAC TCC GAG TTT CAG CAG CTG CTG AAC CAG   1440
          Asp Leu Ala Ser Val Asp Asn Ser Glu Phe Gln Gln Leu Leu Asn Gln
          465             470             475             480

          GGC ATA CCT GTG GCC CCC CAC ACA ACT GAG CCC ATG CTG ATG GAG TAC   1488
          Gly Ile Pro Val Ala Pro His Thr Thr Glu Pro Met Leu Met Glu Tyr
                          485             490             495
  15

          CCT GAG GCT ATA ACT CGC CTA GTG ACA GGG GCC CAG AGG CCC CCC GAC   1536
          Pro Glu Ala Ile Thr Arg Leu Val Thr Gly Ala Gln Arg Pro Pro Asp
                          500             505             510

  20      CCA GCT CCT GCT CCA CTG GGG GCC CCG GGG CTC CCC AAT GGC CTC CTT   1584
          Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly Leu Pro Asn Gly Leu Leu
                          515             520             525

          TCA GGA GAT GAA GAC TTC TCC TCC ATT GCG GAC ATG GAC TTC TCA GCC   1632
  25      Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala Asp Met Asp Phe Ser Ala
                  530             535             540

          CTG CTG AGT CAG ATC AGC TCC TTG GAT CCA CCG GTC GCC ACC ATG GTG   1680
          Leu Leu Ser Gln Ile Ser Ser Leu Asp Pro Pro Val Ala Thr Met Val
  30      545             550             555             560

          AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG   1728
          Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
                          565             570             575
  35

          CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC   1776
          Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly
                  580             585             590

  40      GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC   1824
          Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
                  595             600             605

          ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC   1872
  45      Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
                  610             615             620

          TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC   1920
          Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
  50      625             630             635             640

          GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC   1968
          Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
                          645             650             655
  55

          ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG   2016
```

291

SUBSTITUTE SHEET (RULE 26)

```
          Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
                      660                 665                 670

   5      TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC      2064
          Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
                      675                 680                 685

          TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC      2112
   10     Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
                      690                 695                 700

          AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC      2160
          Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
          705                 710                 715                 720
   15
          AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG      2208
          Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
                      725                 730                 735

   20     CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG      2256
          Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                      740                 745                 750

          CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA      2304
   25     Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
                      755                 760                 765

          GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC      2352
          Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
   30         770                 775                 780

          GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA            2394
          Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
          785                 790                 795
   35
```

(2) INFORMATION FOR SEQ ID NO:141:

   (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 797 amino acids
       (B) TYPE: amino acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

   (ii) MOLECULE TYPE: protein
   (v) FRAGMENT TYPE: internal

   (xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

```
          Met Asp Glu Leu Phe Pro Leu Ile Phe Pro Ala Glu Pro Ala Gln Ala
          1                   5                   10                  15
          Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln Pro Lys Gln Arg Gly Met
                      20                  25                  30
          Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser Ala Gly Ser Ile Pro Gly
                      35                  40                  45
          Glu Arg Ser Thr Asp Thr Thr Lys Thr His Pro Thr Ile Lys Ile Asn
```

```
        50                      55                      60
Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile Ser Leu Val Thr Lys Asp
65                      70                      75                      80
Pro Pro His Arg Pro His Pro His Glu Leu Val Gly Lys Asp Cys Arg
                        85                      90                      95
Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro Asp Arg Cys Ile His Ser
                100                     105                     110
Phe Gln Asn Leu Gly Ile Gln Cys Val Lys Lys Arg Asp Leu Glu Gln
                115                     120                     125
Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn Asn Pro Phe Gln Val Pro
            130                     135                     140
Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu Asn Ala Val Arg Leu Cys
145                     150                     155                     160
Phe Gln Val Thr Val Arg Asp Pro Ser Gly Arg Pro Leu Arg Leu Pro
                165                     170                     175
Pro Val Leu Pro His Pro Ile Phe Asp Asn Arg Ala Pro Asn Thr Ala
                180                     185                     190
Glu Leu Lys Ile Cys Arg Val Asn Arg Asn Ser Gly Ser Cys Leu Gly
                195                     200                     205
Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys Val Gln Lys Glu Asp Ile
            210                     215                     220
Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu Ala Arg Gly Ser Phe Ser
225                     230                     235                     240
Gln Ala Asp Val His Arg Gln Val Ala Ile Val Phe Arg Thr Pro Pro
                245                     250                     255
Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val Arg Val Ser Met Gln Leu
                260                     265                     270
Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu Pro Met Glu Phe Gln Tyr
                275                     280                     285
Leu Pro Asp Thr Asp Asp Arg His Arg Ile Glu Glu Lys Arg Lys Arg
                290                     295                     300
Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys Lys Ser Pro Phe Ser Gly
305                     310                     315                     320
Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg Ile Ala Val Pro Ser Arg
                325                     330                     335
Ser Ser Ala Ser Val Pro Lys Pro Ala Pro Gln Pro Tyr Pro Phe Thr
                340                     345                     350
Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu Phe Pro Thr Met Val Phe
                355                     360                     365
Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala Leu Ala Pro Ala Pro Pro
            370                     375                     380
Gln Val Leu Pro Gln Ala Pro Ala Pro Ala Pro Ala Pro Ala Met Val
385                     390                     395                     400
Ser Ala Leu Ala Gln Ala Pro Ala Pro Val Pro Val Leu Ala Pro Gly
                405                     410                     415
Pro Pro Gln Ala Val Ala Pro Pro Ala Pro Lys Pro Thr Gln Ala Gly
                420                     425                     430
Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln Leu Gln Phe Asp Asp Glu
                435                     440                     445
Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr Asp Pro Ala Val Phe Thr
            450                     455                     460
Asp Leu Ala Ser Val Asp Asn Ser Glu Phe Gln Gln Leu Leu Asn Gln
465                     470                     475                     480
Gly Ile Pro Val Ala Pro His Thr Thr Glu Pro Met Leu Met Glu Tyr
                485                     490                     495
Pro Glu Ala Ile Thr Arg Leu Val Thr Gly Ala Gln Arg Pro Pro Asp
```

SUBSTITUTE SHEET (RULE 26)

294

```
            500                  505                  510
   Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly Leu Pro Asn Gly Leu Leu
            515                  520                  525
   Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala Asp Met Asp Phe Ser Ala
5           530                  535                  540
   Leu Leu Ser Gln Ile Ser Ser Leu Asp Pro Pro Val Ala Thr Met Val
   545                  550                  555                  560
   Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
                        565                  570                  575
10 Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly
   .        580                  585                  590
   Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
            595                  600                  605
   Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
15          610                  615                  620
   Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
   625                  630                  635                  640
   Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
                        645                  650                  655
20 Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
                        660                  665                  670
   Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
                        675                  680                  685
   Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
25          690                  695                  700
   Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
   705                  710                  715                  720
   Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
                        725                  730                  735
30 Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                        740                  745                  750
   Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
                        755                  760                  765
   Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
35 770                  775                  780
   Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
   785                  790                  795
```

            (2) INFORMATION FOR SEQ ID NO:142:
40

            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 2394 base pairs
                (B) TYPE: nucleic acid
                (C) STRANDEDNESS: single
45   (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: cDNA
            (ix) FEATURE:

50   (A) NAME/KEY: Coding Sequence
                (B) LOCATION: 1...2391
                (D) OTHER INFORMATION:

            (xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:
55

   ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG   48

SUBSTITUTE SHEET (RULE 26)

295

```
      Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
      1               5               10                  15

  5   GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
      Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                  20              25                  30

      GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
      Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
 10               35              40                  45

      TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
      Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                  50              55                  60
 15
      CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
      Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
      65                  70              75                  80

 20   CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
      Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                      85              90                  95

      CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
 25   Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                  100             105                 110

      GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
      Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 30               115             120                 125

      ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
      Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                  130             135                 140
 35
      AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
      Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
      145                 150                 155                 160

 40   GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
      Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                      165             170                 175

      GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
 45   Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                  180             185                 190

      CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
      Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
 50               195             200                 205

      AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
      Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                  210             215                 220
 55
      GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
```

295

SUBSTITUTE SHEET (RULE 26)

```
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                 230             235                 240

 5   GGA CTC AGA TCT CGA GCC ATG GAC GAA CTG TTC CCC CTC ATC TTC CCG   768
     Gly Leu Arg Ser Arg Ala Met Asp Glu Leu Phe Pro Leu Ile Phe Pro
                     245             250                 255

     GCA GAG CCA GCC CAG GCC TCT GGC CCC TAT GTG GAG ATC ATT GAG CAG   816
     Ala Glu Pro Ala Gln Ala Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln
 10                  260             265             270

     CCC AAG CAG CGG GGC ATG CGC TTC CGC TAC AAG TGC GAG GGG CGC TCC   864
     Pro Lys Gln Arg Gly Met Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser
                 275             280             285
 15
     GCG GGC AGC ATC CCA GGC GAG AGG AGC ACA GAT ACC ACC AAG ACC CAC   912
     Ala Gly Ser Ile Pro Gly Glu Arg Ser Thr Asp Thr Thr Lys Thr His
                 290             295             300

 20  CCC ACC ATC AAG ATC AAT GGC TAC ACA GGA CCA GGG ACA GTG CGC ATC   960
     Pro Thr Ile Lys Ile Asn Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile
     305                 310             315                 320

     TCC CTG GTC ACC AAG GAC CCT CCT CAC CGG CCT CAC CCC CAC GAG CTT  1008
 25  Ser Leu Val Thr Lys Asp Pro Pro His Arg Pro His Pro His Glu Leu
                     325             330             335

     GTA GGA AAG GAC TGC CGG GAT GGC TTC TAT GAG GCT GAG CTC TGC CCG  1056
     Val Gly Lys Asp Cys Arg Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro
 30                  340             345             350

     GAC CGC TGC ATC CAC AGT TTC CAG AAC CTG GGA ATC CAG TGT GTG AAG  1104
     Asp Arg Cys Ile His Ser Phe Gln Asn Leu Gly Ile Gln Cys Val Lys
                 355             360             365
 35
     AAG CGG GAC CTG GAG CAG GCT ATC AGT CAG CGC ATC CAG ACC AAC AAC  1152
     Lys Arg Asp Leu Glu Gln Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn
                 370             375             380

 40  AAC CCC TTC CAA GTT CCT ATA GAA GAG CAG CGT GGG GAC TAC GAC CTG  1200
     Asn Pro Phe Gln Val Pro Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu
     385                 390             395                 400

     AAT GCT GTG CGG CTC TGC TTC CAG GTG ACA GTG CGG GAC CCA TCA GGC  1248
 45  Asn Ala Val Arg Leu Cys Phe Gln Val Thr Val Arg Asp Pro Ser Gly
                     405             410             415

     AGG CCC CTC CGC CTG CCG CCT GTC CTT CCT CAT CCC ATC TTT GAC AAT  1296
     Arg Pro Leu Arg Leu Pro Pro Val Leu Pro His Pro Ile Phe Asp Asn
 50                  420             425             430

     CGT GCC CCC AAC ACT GCC GAG CTC AAG ATC TGC CGA GTG AAC CGA AAC  1344
     Arg Ala Pro Asn Thr Ala Glu Leu Lys Ile Cys Arg Val Asn Arg Asn
                 435             440             445
 55
     TCT GGC AGC TGC CTC GGT GGG GAT GAG ATC TTC CTA CTG TGT GAC AAG  1392
```

296

BNSDOCID: <WO___9845704A2_I_>

```
      Ser Gly Ser Cys Leu Gly Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys
          450             455             460

 5    GTG CAG AAA GAG GAC ATT GAG GTG TAT TTC ACG GGA CCA GGC TGG GAG   1440
      Val Gln Lys Glu Asp Ile Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu
      465             470             475             480

      GCC CGA GGC TCC TTT TCG CAA GCT GAT GTG CAC CGA CAA GTG GCC ATT   1488
10    Ala Arg Gly Ser Phe Ser Gln Ala Asp Val His Arg Gln Val Ala Ile
                      485             490             495

      GTG TTC CGG ACC CCT CCC TAC GCA GAC CCC AGC CTG CAG GCT CCT GTG   1536
      Val Phe Arg Thr Pro Pro Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val
                  500             505             510
15
      CGT GTC TCC ATG CAG CTG CGG CGG CCT TCC GAC CGG GAG CTC AGT GAG   1584
      Arg Val Ser Met Gln Leu Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu
              515             520             525

20    CCC ATG GAA TTC CAG TAC CTG CCA GAT ACA GAC GAT CGT CAC CGG ATT   1632
      Pro Met Glu Phe Gln Tyr Leu Pro Asp Thr Asp Asp Arg His Arg Ile
              530             535             540

      GAG GAG AAA CGT AAA AGG ACA TAT GAG ACC TTC AAG AGC ATC ATG AAG   1680
25    Glu Glu Lys Arg Lys Arg Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys
      545             550             555             560

      AAG AGT CCT TTC AGC GGA CCC ACC GAC CCC CGG CCT CCA CCT CGA CGC   1728
      Lys Ser Pro Phe Ser Gly Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg
30                    565             570             575

      ATT GCT GTG CCT TCC CGC AGC TCA GCT TCT GTC CCC AAG CCA GCA CCC   1776
      Ile Ala Val Pro Ser Arg Ser Ser Ala Ser Val Pro Lys Pro Ala Pro
                  580             585             590
35
      CAG CCC TAT CCC TTT ACG TCA TCC CTG AGC ACC ATC AAC TAT GAT GAG   1824
      Gln Pro Tyr Pro Phe Thr Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu
                  595             600             605

40    TTT CCC ACC ATG GTG TTT CCT TCT GGG CAG ATC AGC CAG GCC TCG GCC   1872
      Phe Pro Thr Met Val Phe Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala
              610             615             620

      TTG GCC CCG GCC CCT CCC CAA GTC CTG CCC CAG GCT CCA GCC CCT GCC   1920
45    Leu Ala Pro Ala Pro Pro Gln Val Leu Pro Gln Ala Pro Ala Pro Ala
      625             630             635             640

      CCT GCT CCA GCC ATG GTA TCA GCT CTG GCC CAG GCC CCA GCC CCT GTC   1968
      Pro Ala Pro Ala Met Val Ser Ala Leu Ala Gln Ala Pro Ala Pro Val
50                    645             650             655

      CCA GTC CTA GCC CCA GGC CCT CCT CAG GCT GTG GCC CCA CCT GCC CCC   2016
      Pro Val Leu Ala Pro Gly Pro Pro Gln Ala Val Ala Pro Pro Ala Pro
                  660             665             670
55
      AAG CCC ACC CAG GCT GGG GAA GGA ACG CTG TCA GAG GCC CTG CTG CAG   2064
```

298

```
     Lys Pro Thr Gln Ala Gly Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln
             675                 680                 685

     CTG CAG TTT GAT GAT GAA GAC CTG GGG GCC TTG CTT GGC AAC AGC ACA    2112
  5  Leu Gln Phe Asp Asp Glu Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr
             690                 695                 700

     GAC CCA GCT GTG TTC ACA GAC CTG GCA TCC GTC GAC AAC TCC GAG TTT    2160
     Asp Pro Ala Val Phe Thr Asp Leu Ala Ser Val Asp Asn Ser Glu Phe
 10  705                 710                 715                 720

     CAG CAG CTG CTG AAC CAG GGC ATA CCT GTG GCC CCC CAC ACA ACT GAG    2208
     Gln Gln Leu Leu Asn Gln Gly Ile Pro Val Ala Pro His Thr Thr Glu
                     725                 730                 735
 15
     CCC ATG CTG ATG GAG TAC CCT GAG GCT ATA ACT CGC CTA GTG ACA GGG    2256
     Pro Met Leu Met Glu Tyr Pro Glu Ala Ile Thr Arg Leu Val Thr Gly
                     740                 745                 750

 20  GCC CAG AGG CCC CCC GAC CCA GCT CCT GCT CCA CTG GGG GCC CCG GGG    2304
     Ala Gln Arg Pro Pro Asp Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly
                     755                 760                 765

     CTC CCC AAT GGC CTC CTT TCA GGA GAT GAA GAC TTC TCC TCC ATT GCG    2352
 25  Leu Pro Asn Gly Leu Leu Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala
                     770                 775                 780

     GAC ATG GAC TTC TCA GCC CTG CTG AGT CAG ATC AGC TCC TAA            2394
     Asp Met Asp Phe Ser Ala Leu Leu Ser Gln Ile Ser Ser
 30  785                 790                 795
```

```
                (2)  INFORMATION FOR SEQ ID NO:143:

 35             (i)  SEQUENCE CHARACTERISTICS:
                    (A)  LENGTH: 797 amino acids
                    (B)  TYPE: amino acid
                    (C)  STRANDEDNESS: single
                    (D)  TOPOLOGY: linear
 40
                (ii)  MOLECULE TYPE: protein
                (v)  FRAGMENT TYPE: internal

                (xi)  SEQUENCE DESCRIPTION: SEQ ID NO:143:
 45
     Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
       1               5                  10                 15
     Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
                     20                  25                 30
 50  Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
                 35                  40                  45
     Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
                 50                  55                  60
     Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
 55  65                  70                  75                 80
     Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
```

298

299

```
                    85                    90                      95
     Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
                    100                   105                110
     Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 5                  115                   120                125
     Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
                    130                   135                140
     Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
                    145                   150                155                160
10   Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                    165                   170                175
     Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
                    180                   185                190
     Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
15                  195                   200                205
     Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
                    210                   215                220
     Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
     225                230                235                240
20   Gly Leu Arg Ser Arg Ala Met Asp Glu Leu Phe Pro Leu Ile Phe Pro
                    245                   250                255
     Ala Glu Pro Ala Gln Ala Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln
                    260                   265                270
     Pro Lys Gln Arg Gly Met Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser
25                  275                   280                285
     Ala Gly Ser Ile Pro Gly Glu Arg Ser Thr Asp Thr Thr Lys Thr His
                    290                   295                300
     Pro Thr Ile Lys Ile Asn Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile
     305                310                315                320
30   Ser Leu Val Thr Lys Asp Pro Pro His Arg Pro His Pro His Glu Leu
                    325                   330                335
     Val Gly Lys Asp Cys Arg Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro
                    340                   345                350
     Asp Arg Cys Ile His Ser Phe Gln Asn Leu Gly Ile Gln Cys Val Lys
35                  355                   360                365
     Lys Arg Asp Leu Glu Gln Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn
                    370                   375                380
     Asn Pro Phe Gln Val Pro Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu
     385                390                   395                400
40   Asn Ala Val Arg Leu Cys Phe Gln Val Thr Val Arg Asp Pro Ser Gly
                    405                   410                415
     Arg Pro Leu Arg Leu Pro Pro Val Leu Pro His Pro Ile Phe Asp Asn
                    420                   425                430
     Arg Ala Pro Asn Thr Ala Glu Leu Lys Ile Cys Arg Val Asn Arg Asn
45                  435                   440                445
     Ser Gly Ser Cys Leu Gly Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys
                    450                   455                460
     Val Gln Lys Glu Asp Ile Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu
     465                470                   475                480
50   Ala Arg Gly Ser Phe Ser Gln Ala Asp Val His Arg Gln Val Ala Ile
                    485                   490                495
     Val Phe Arg Thr Pro Pro Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val
                    500                   505                510
     Arg Val Ser Met Gln Leu Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu
55                  515                   520                525
     Pro Met Glu Phe Gln Tyr Leu Pro Asp Thr Asp Asp Arg His Arg Ile
```

299

```
                     530                    535                    540
        Glu Glu Lys Arg Lys Arg Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys
        545                    550                    555                    560
  5     Lys Ser Pro Phe Ser Gly Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg
                         565                    570                    575
        Ile Ala Val Pro Ser Arg Ser Ser Ala Ser Val Pro Lys Pro Ala Pro
                     580                    585                    590
        Gln Pro Tyr Pro Phe Thr Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu
                     595                    600                    605
  10    Phe Pro Thr Met Val Phe Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala
                     610                    615                    620
        Leu Ala Pro Ala Pro Pro Gln Val Leu Pro Gln Ala Pro Ala Pro Ala
        625                    630                    635                    640
        Pro Ala Pro Ala Met Val Ser Ala Leu Ala Gln Ala Pro Ala Pro Val
  15                     645                    650                    655
        Pro Val Leu Ala Pro Gly Pro Pro Gln Ala Val Ala Pro Pro Ala Pro
                         660                    665                    670
        Lys Pro Thr Gln Ala Gly Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln
                     675                    680                    685
  20    Leu Gln Phe Asp Asp Glu Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr
                     690                    695                    700
        Asp Pro Ala Val Phe Thr Asp Leu Ala Ser Val Asp Asn Ser Glu Phe
        705                    710                    715                    720
        Gln Gln Leu Leu Asn Gln Gly Ile Pro Val Ala Pro His Thr Thr Glu
  25                     725                    730                    735
        Pro Met Leu Met Glu Tyr Pro Glu Ala Ile Thr Arg Leu Val Thr Gly
                         740                    745                    750
        Ala Gln Arg Pro Pro Asp Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly
                     755                    760                    765
  30    Leu Pro Asn Gly Leu Leu Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala
                     770                    775                    780
        Asp Met Asp Phe Ser Ala Leu Leu Ser Gln Ile Ser Ser
        785                    790                    795
```

CLAIMS

1. A method for extracting quantitative information relating to an influence on a cellular response, the method comprising recording variation, caused by the influence on a mechanically intact living cell or mechanically intact living cells, in spatially distributed light emitted from a luminophore, the luminophore being present in the cell or cells and being capable of being redistributed in a manner which is related with the degree of the influence, and/or of being modulated by a component which is capable of being redistributed in a manner which is related to the degree of the influence, the association resulting in a modulation of the luminescence characteristics of the luminophore, and processing the recorded variation in the spatially distributed light to provide quantitative information correlating the spatial distribution to the degree of the influence on the cellular response.

2. A method according to claim 1, as used for extracting quantitative information relating to an influence on an intracellular pathway involving redistribution of at least one component associated with the pathway, or part thereof, the method comprising recording the result of the influence on mechanically intact living cell or cells, as manifested in spatially distributed light emitted from a luminophore which is present in the cell or cells and which is capable of being redistributed, by modulation of the pathway, in a manner which is related to the redistribution of the at least one component of the intracellular pathway, processing the recorded result to provide quantitative information about the spatially distributed light and correlating the quantitative information to the degree of the influence on the intracellular pathway.

3. A method according to claim 1 or 2, wherein the quantitative information which is indicative of the degree of the cellular response to the influence or the result of the influence on the intracellular pathway is extracted from the recording or recordings according to a predetermined calibration based on responses or results, recorded in the same manner, to known degrees of a relevant specific influence.

4. A method according to any of the preceding claims, wherein the influence is contact between the mechanically intact living cell or the group of mechanically intact living cells with a

chemical substance and/or incubation of the mechanically intact living cell or the group of mechanically intact living cells with a chemical substance.

5. A method according to claim 4 wherein the substance is a substance whose effect on an intracellular pathway is to be determined.

6. A method according to any of the preceding claims, wherein the recording is made at a single point in time after the application of the influence.

7. A method according to any of claims 1-5, wherein the recording is made at two points in time, one point being before, and the other point being after the application of the influence.

8. A method according to any of claims 1-5, wherein the recording is performed at a series of points in time, in which the application of the influence occurs at some time after the first time point in the series of recordings, the recording being performed, e.g., with a predetermined time spacing of from 0.1 seconds to 1 hour, preferably from 1 to 60 seconds, more preferably from 1 to 30 seconds, in particular from 1 to 10 seconds, over a time span of from 1 second to 12 hours, such as from 10 seconds to 12 hours, e.g., from 10 seconds to one hour, such as from 60 seconds to 30 minutes or 20 minutes.

9. A method according to any of claims 1-7, wherein the cell or cells is/are fixed at a point in time after the application of the influence at which the response has been predetermined to be significant, and the recording is made at an arbitrary later time.

10. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of being redistributed in a manner which is physiologically relevant to the degree of the influence.

11. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of associating with a component which is capable of being redistributed in manner which is physiologically relevant to the degree of the influence.

5   12. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of being redistributed in a manner which is experimentally determined to be correlated to the degree of the influence.

13. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of being redistributed, by modulation of the intracellular pathway, in substantially the same manner as the at least one component of the intracellular pathway.

14. A method according to any of claims 1-13, wherein the luminophore is a luminophore which is capable of being quenched upon spatial association with a component which is redistributed by modulation of the pathway, the quenching being measured as a decrease in the intensity of the luminescence.

15. A method according to any of claims 1-13, wherein the variation or result with respect to the spatially distributed light emitted by the luminophore is detected by a change in the resonance energy transfer between the luminophore and another luminescent entity capable of delivering energy to the luminophore, each of which has been selected or engineered to become part of, bound to or associated with particular components of the intracellular pathway, and one of which undergoes redistribution in response to the influence, thereby changing the amount of resonance energy transfer, the change in the resonance energy transfer being measured as a change in the intensity of emission from the luminophore.

16. A method according to claim 15, wherein the change in the intensity of the emission from the luminophore is sensed by a single channel photodetector which responds only to the average intensity of the luminophore in a non-spatially resolved fashion

17. A method according to any of claims 1-16, wherein the property of the light being re-corded is intensity, fluorescence lifetime, polarization, wavelength shift, or other property which is modulated as a result of the underlying cellular response.

5

18. A method according to any of claims 1-15 or 17, wherein the recording of the spatially distributed light is performed using a recording system which records the spatial distribution of a recordable property of the light in the form of an ordered array of values.

10   19. A method according to claim 18, wherein the recording of the spatial distribution of the recordable property of the light is performed using a charge transfer device such as a CCD array or a vacuum tube device such as a vidicon tube.

20. A method according to any of the preceding claims, wherein the light to be measured

15   passes through a filter which selects the desired component of the light to be measured and rejects other components.

21. A method according to any of the preceding claims, wherein the recording of the spatial distribution of the recordable property of light is performed by fluorescence microscopy.

20

22. A method according to any of the preceding claims, wherein the recording of the varia-tion or result with respect to light emitted from the luminophore is performed by recording the spatially distributed light as one or more digital images, and the processing of the recorded variation to reduce it to one or more numbers representative of the degree of redistribution

25   comprises a digital image processing procedure or combination of digital image processing procedures.

23. A method according to any of claims 2-22, wherein the intracellular pathway is an intra-cellular signalling pathway.

24. A method according to any of the preceding claims, wherein the luminophore is a fluorophore.

5   25. A method according to any of the preceding claims wherein the luminophore is a polypeptide encoded by and expressed from a nucleotide sequence harboured in the cell or cells.

26. A method according to any of the preceding claims, wherein the luminophore is a hybrid
10 polypeptide comprising a fusion of at least a portion of each of two polypeptides one of which comprises a luminescent polypeptide and the other one of which comprises a biologically active polypeptide, as defined herein.

27. A method according to claim 26, wherein the luminescent polypeptide is a GFP as de-
15 fined herein.

28. A method according to claim 27 wherein the GFP is selected from the group consisting of green fluorescent proteins having the F64L mutation as defined herein.

20 29. A method according to claim 28 wherein the GFP is a GFP variant selected from the group consisting of F64L-GFP, F64L-Y66H-GFP, F64L-S65T-GFP, and EGFP.

30. A method according to any of the previous claims for detecting intracellular translocation of a biologically active polypeptide affecting intracellular processes upon activation, the
25 method comprising

    a) culturing one or more cells containing a nucleotide sequence coding for a hybrid polypeptide comprising a GFP which is N- or C-terminally tagged, optionally through a linker, to a biologically active polypeptide under conditions permitting expression of the nucleotide sequence,

b) modulating the activity of the biologically active polypeptide by incubating the cell or cells with a substance having biological activity and

c) measuring the fluorescence produced by the incubated cell or cells and determining the result or variation with respect to the fluorescence, such result or variation being indicative of the translocation of a biologically active polypeptide in said cell.

31. A method according to claim 30, wherein the nucleotide sequence is a DNA sequence.

32. A method according to claim 30 or 31, wherein the modulation is an activation.

33. A method according to claim 30 or 31, wherein the modulation is a deactivation.

34. A method according to any of claims 30-33 wherein the fluorescence of the cell or cells is measured prior to the modulation, and the result or variation determined in step (c) is a change in fluorescence compared to the fluorescence measured prior to the modulation.

35. A method according to any of claims 30-34, wherein the intracellular processes are intra-cellular signalling pathways.

36. A method according to claim 34, wherein the change in fluorescence measured in step (c) comprises determining a change in the spatial distribution of the fluorescence.

37. A method according to any of the preceding claims wherein the mechanically intact living cell or cells is/are a mammalian cell/mammalian cells which, during the time peroid over which the influence is observed, is/are incubated at a temperature of 30°C or above, pref-erably at a temperature of from 32°C to 39°C, more preferably at a temperature of from 35°C to 38°C, and most preferably at a temperature of about 37°C.

38. A method according to any of the preceding claims, wherein the at least one mechanically intact living cell is part of a matrix of identical or non-identical cells.

39. A method according to any of claims 1-36 and 38, wherein the cell or cells is/are se-
5 lected from the group consisting of fungal cells, such as a yeast cell; invertebrate cells including insect cells; and vertebrate cells, such as mammalian cells.

40. A nucleic acid construct coding for a fusion polypeptide comprising a biologically active polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and
10 a GFP, with the proviso that the construct is not a construct coding for a fusion polypeptide in which the biologically active polypeptide is selected from the group consisting of PKC-alpha, PKC-gamma, and PKC-epsilon.

41. A nucleic acid construct coding for a fusion polypeptide comprising a biologically active
15 polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and an F64L mutant of GFP.

42. A nucleic acid construct according to claim 40 or 41, wherein the biologically active polypeptide is a protein kinase or a phosphatase.

20

43. A nucleic acid construct according to any of claims 40-42 wherein the GFP is N- or C-terminally tagged, optionally via a peptide linker, to the biologically active polypeptide or part thereof.

25 44. A nucleic acid construct according to any of claims 40, 41 and 43, wherein the biologically active polypeptide is a transcription factor or a part thereof which changes cellular localisation upon activation.

308

45. A nucleic acid construct according to any of claims 40, 41 and 43, wherein the biologi-
cally active polypeptide is a protein, or a part thereof, which is associated with the cy-
toskeletal network and which changes cellular localisation upon activation.

5   46. A nucleic acid construct according to any of claims 40-43, wherein the biologically active
polypeptide is a protein kinase or a part thereof which changes cellular localisation upon ac-
tivation.

47. A nucleic acid construct according to claim 46, wherein the protein kinase is a ser-
10   ine/threonine protein kinase or a part thereof capable of changing intracellular localisation
upon activation.

48. A nucleic acid construct according to claim 46, wherein the protein kinase is a tyrosine
protein kinase or a part thereof capable of changing intracellular localisation upon activation.

15

49. A nucleic acid construct according to claim 46, wherein the protein kinase is a phosphol-
ipid-dependent serine/threonine protein kinase or a part thereof capable of changing intra-
cellular localisation upon activation.

20   50. A nucleic acid construct according to claim 46, wherein the protein kinase is a cAMP-
dependent protein kinase or a part thereof capable of changing cellular localisation upon ac-
tivation.

51. A nucleic acid construct according to claim 50 which codes for a PKAc-F64L-S65T-GFP
25   fusion.

52. A nucleic acid construct according to claim 46, wherein the protein kinase is a cGMP-
dependent protein kinase or a part thereof capable of changing cellular localisation upon ac-
tivation.

53. A nucleic acid construct according to claim 46, wherein the protein kinase is a calmodulin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

5

54. A nucleic acid construct according to claim 46, wherein the protein kinase is a mitogen-activated serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

10   55. A nucleic acid construct according to claim 54, which codes for an ERK1-F64L-S65T-GFP fusion.

56. A nucleic acid construct according to claim 54, which codes for an EGFP-ERK1 fusion.

15   57. A nucleic acid construct according to claim 46, wherein the protein kinase is a cyclin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

58. A nucleic acid construct according to claim 42 or 43, wherein the biologically active
20   polypeptide is a protein phosphatase or a part thereof capable of changing cellular localisation upon activation.

59. A nucleic acid construct according to any of claims 40-58 which is a DNA construct.

25   60. A nucleic acid construct according to any of claims 40-59 wherein the gene encoding GFP is derived from Aequorea victoria.

61. A nucleic acid construct according to claim 60 in which the gene encoding GFP is the gene encoding EGFP as defined herein.

62. A nucleic acid construct according to claim 60 in which the gene encoding a GFP is a gene encoding a GFP variant selected from F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP.

5

63. A DNA construct according to claim 59 and 61 or, where applicable, 62, which is a construct as identified by any of the DNA sequences shown in SEQ ID NO: 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, and 142, or is a variant thereof ca-
10   pable of encoding the same fusion polypeptide or a fusion polypeptide which is biologically equivalent thereto, as defined herein.

64. A cell containing a nucleic acid construct according to any of claims 40-63 and capable of expressing the sequence encoded by the construct.

15

65. A cell according to claim 64, which is a eukaryotic cell.

66. A cell according to claim 64, which is selected from the group consisting of fungal cells, such as yeast cells; invertebrate cells, including insect cells, and vertebrate cells, such as
20   mammalian cells.

67. A cell according to claim 66, which is a mammalian cell.

68. An organism carrying in at least one of its component cells a nucleic acid sequence as
25   contained in the constructs according to any of claims 40-59, said cell being capable of expressing said nucleic acid sequence.

69. An organism according to claim 68 which is selected from the group consisting of unicellular and multicellular organisms, such as a mammal.

70. A fluorescent probe comprising a GFP which is N- or C-terminally tagged, optionally via a peptide linker, to a biologically active polypeptide or a part or a subunit thereof which is a component of a intracellular signalling pathway as defined herein, the probe being a probe

5   which is encoded by the nucleic acid construct according to any of claims 40-59.

71. A method according to any of claims 1-39, wherein the luminophore is a fusion polypeptide as encoded by the nucleic acid construct according to any of claims 40-63.

10   72. A method according to any of claims 1-39 or 71 in which the method of the invention is used in a screening program as defined herein.

73. An apparatus for measuring the distribution of fluorescence in at least one cell, and thereby any change in the distribution of fluorescence in at least one cell, which includes the

15   following component parts: (a) a light source, (b) a means for selecting the wavelength(s) of light from the source which will excite the fluorescence of the protein, (c) a means for rapidly blocking or pass ing the excitation light into the rest of the system, (d) a series of optical elements for conveying the excitation light to the specimen, collecting the emitted fluorescence in a spatially resolved fashion, and forming an image from this fluorescence, (e) a

20   bench or stand which holds the container of the cells being measured in a predetermined geometry with respect to the series of optical elements, (f) a detector to record the spatially resolved fluorescence in the form of an image, (g) a computer or electronic system and associated software to acquire and store the recorded images, and to compute the degree of redistribution from the recorded images.

25

74. An apparatus according to claim 73 in which some or all of the system is automated.

75. An apparatus according to claim 73 in which components d and e comprise a fluorescence microscope.

30

312

76. An apparatus according to claim 73 in which component f is a CCD camera.

77. An apparatus according to claim 73 in which the image is formed and recorded by an optical scanning system.

5

78. An apparatus according to claim 73 in which a liquid addition system is used to add a known or unknown compound to any or all of the cells in the cell holder at a time determined in advance.

10   79. An apparatus according to claim 78 in which the liquid addition system is under the control of the computer or electronic system.

80. A method according to any of claims 1-79 wherein the method is a screening program for the identification of a biologically active substance as defined herein that directly or indirectly

15   affects an intracellular signalling pathway and is potentially useful as a medicament, wherein the result of the individual measurement of each substance being screened which indicates its potential biological activity is based on measurement of the redistribution of spatially resolved luminescence in living cells and which undergoes a change in distribution upon activation of an intracellular signalling pathway.

20

81 A method according to any of claims 1-79 wherein the method is a screening program for the identification of a biologically toxic substance as defined herein that exerts its toxic effect by interfering with an intracellular signalling pathway, wherein the result of the individual measurement of each substance being screened which indicates its potential biologically

25   toxic activity is based on measurement of the redistribution of said fluorescent probe in living cells and which undergoes a change in distribution upon activation of an intracellular signalling pathway.

82. A method according to any of claims 1-80 wherein a fluorescent probe is used in back-
30   tracking of signal transduction pathways as defined herein.

83. A method of treating a condition or disease related to the intracellular function of a protein kinase comprising administering to a patient suffering from said condition or disease an effective amount of a compound which has been discovered by any method according to the

5   invention.

84. A compound that modulates a component of an intracellular pathway as defined herein, as determined by a method according to the method of the invention.

10   85. A medical composition comprising a therapeutic amount of a compound identified according the method of the invention.

86. A method of selectively treating a patient suffering from an ailment which responds to medical treatment comprising obtaining a primary cell or cells from said patient, transfecting

15   the cell or cells with at least one DNA sequence encoding a fluorescent probe according to the invention, culturing the cell or cells under conditions permitting the expression of said probes and exposing it to an array of medicaments suspected of being capable of alleviating said ailment, then comparing changes in fluorescence patterns or redistribution patterns of the fluorescent probes in the intact living cell or cells to detect the cellular response to the

20   specific medicaments (obtaining a cellular action profile), then selecting a medicament(s) based on desired activity and acceptable level of side effects and administering an effective amount of said medicament(s) to said patient.

87. A method according to any of claims 1-80 of identifying a drug target among the group of

25   biologically active polypeptides which are components of intracellular signalling pathways.

Fig 1

a)

b)

c)

d)

Fig 2

i   ii   iii

iv   v   vi
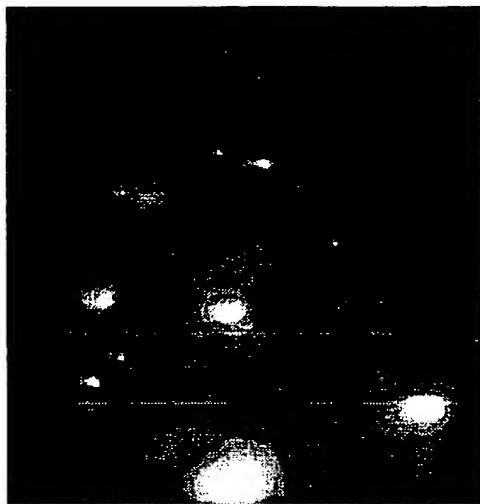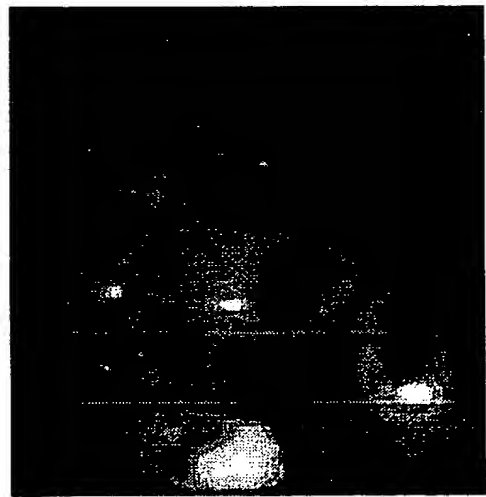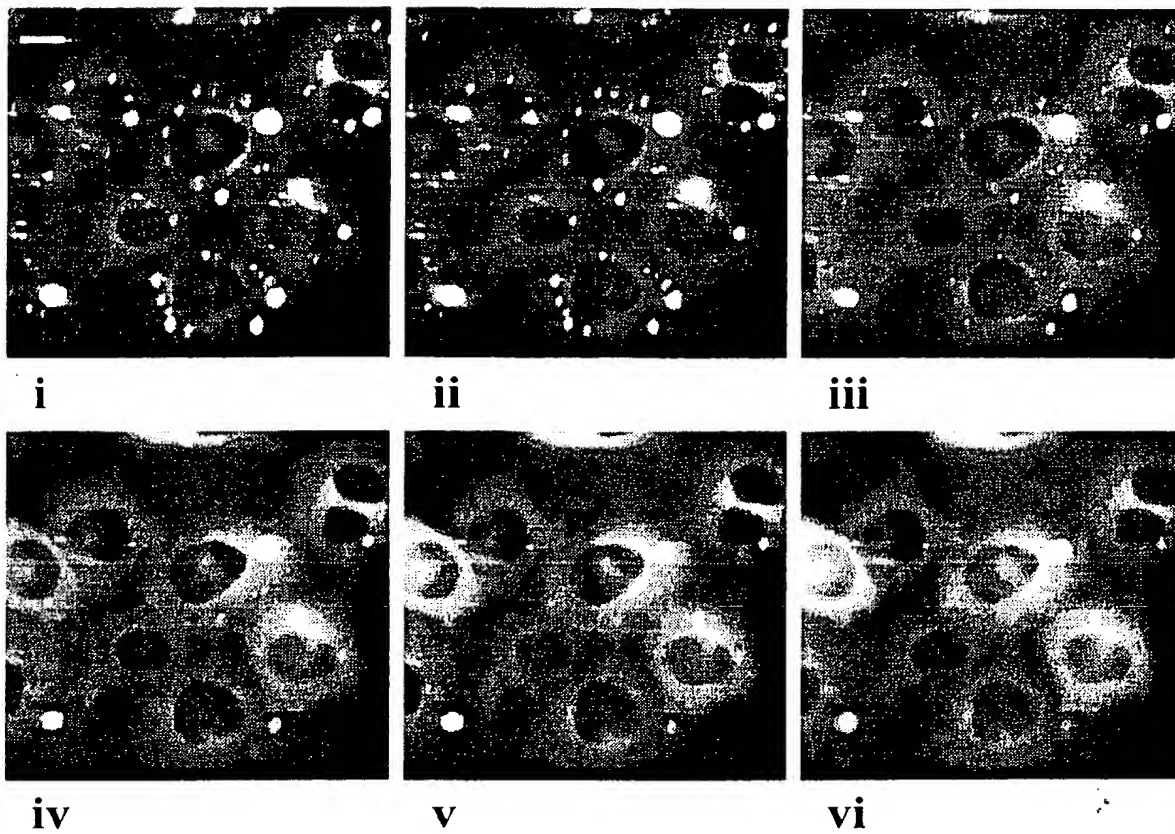
Fig 3
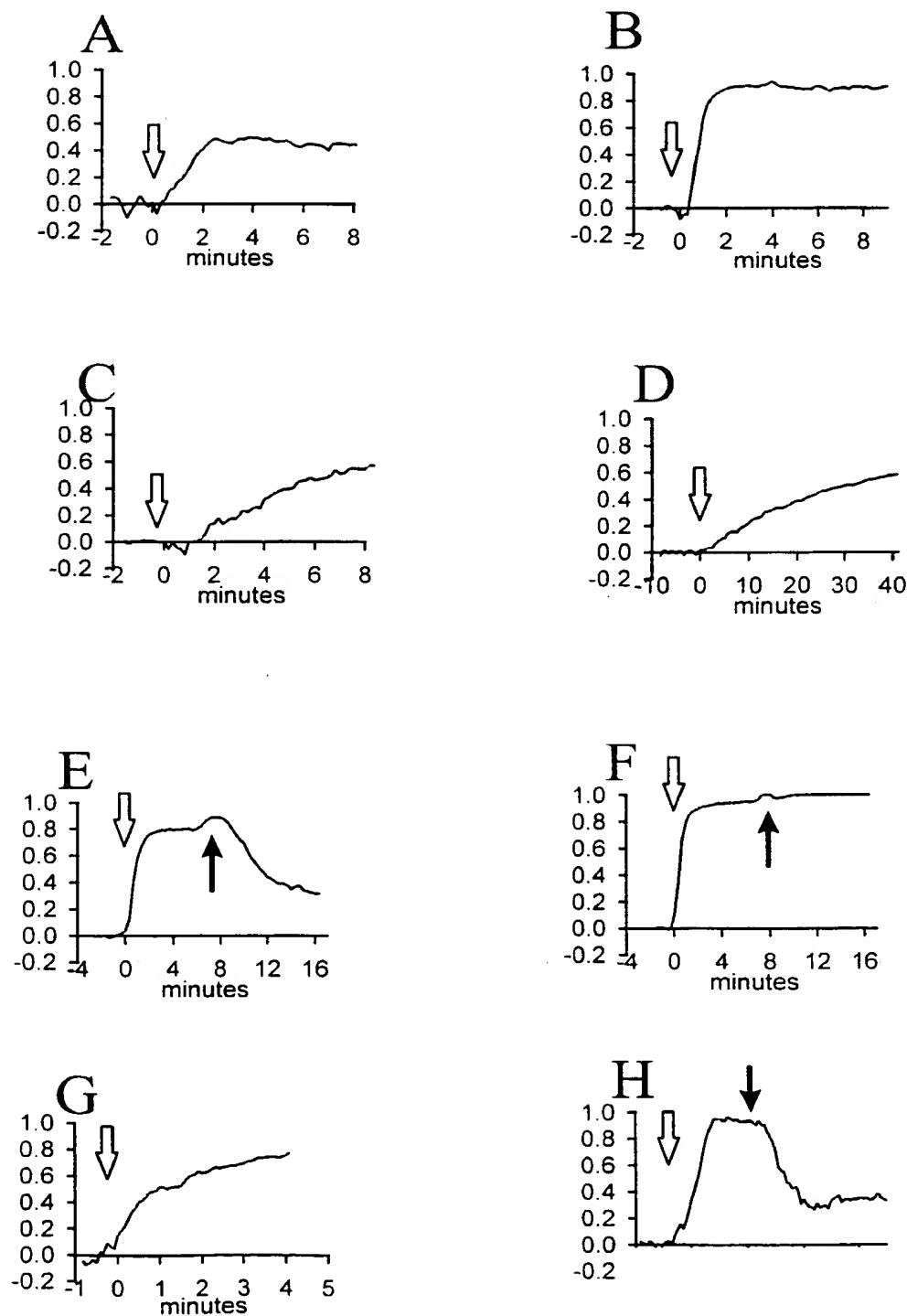
Fig 4
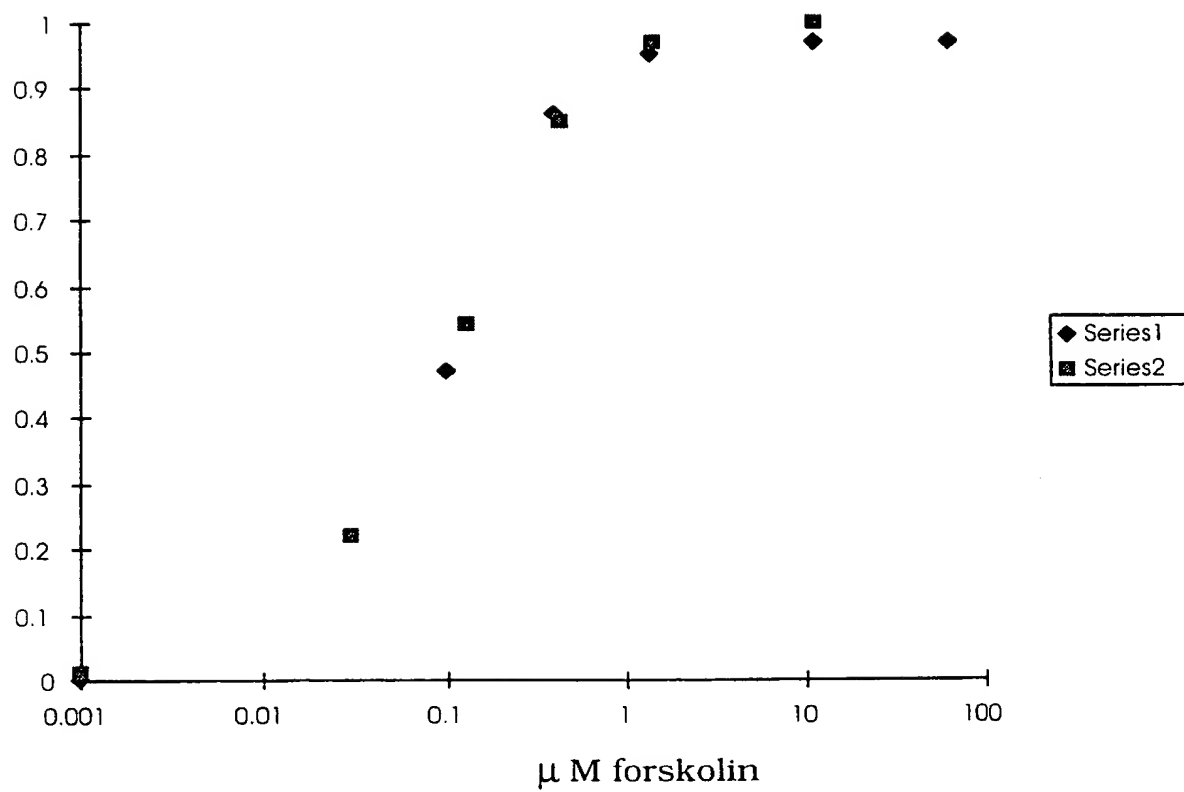
μ M forskolin

Fig 5

[forskolin]μM	$t_{1/2max}$ / s	t_{max} / s
1	115±21	310±31
10	69±14	224±47
50	47±10	125±28

Fig 6

Fig 7

a)

b)

c)

Fig 8

Fig 9

a)

b)

c)

d)

Fig 10

a)

b)

c)

Fig 11

5μm
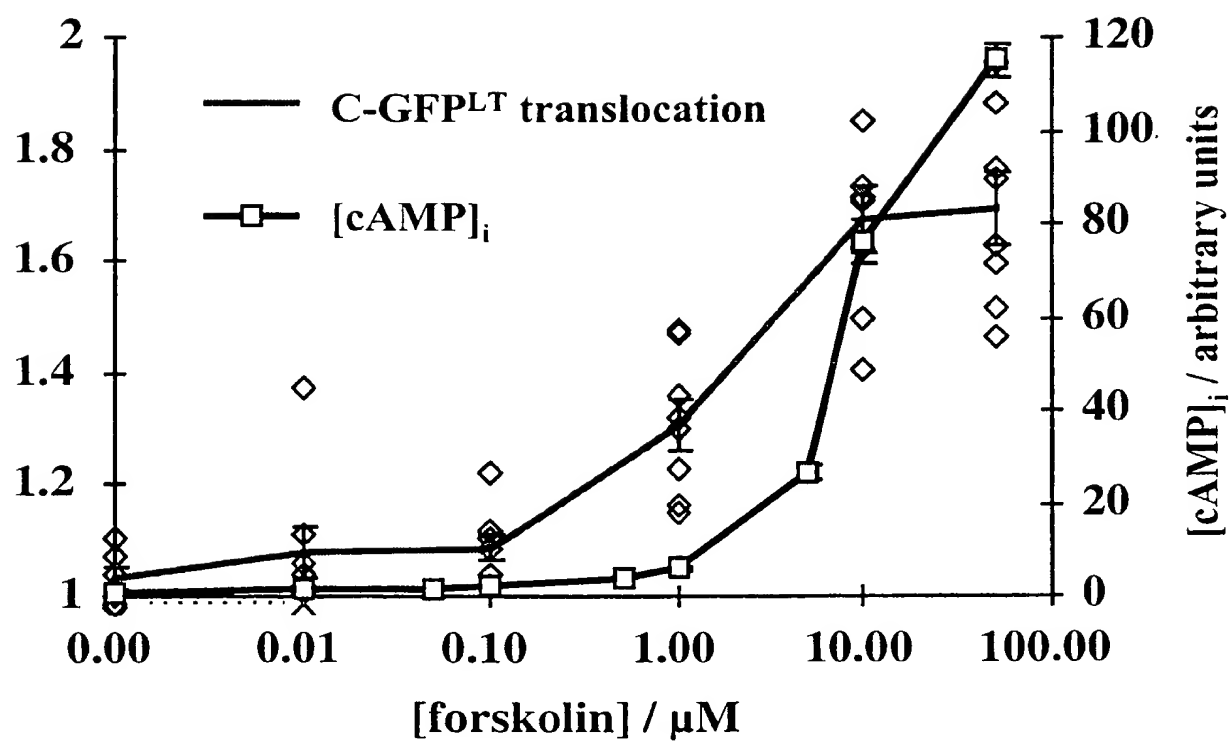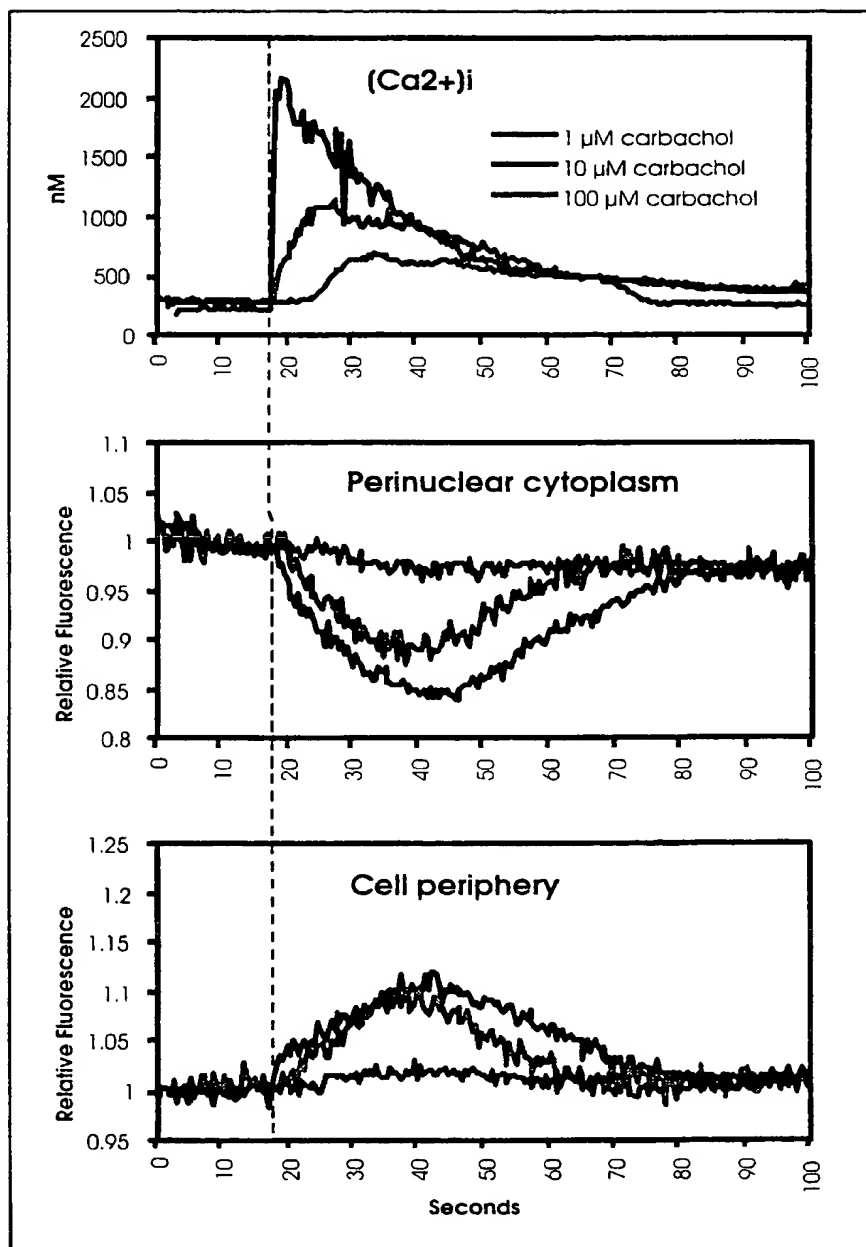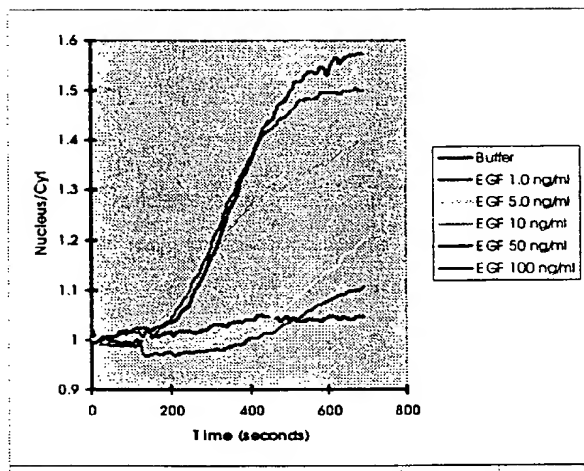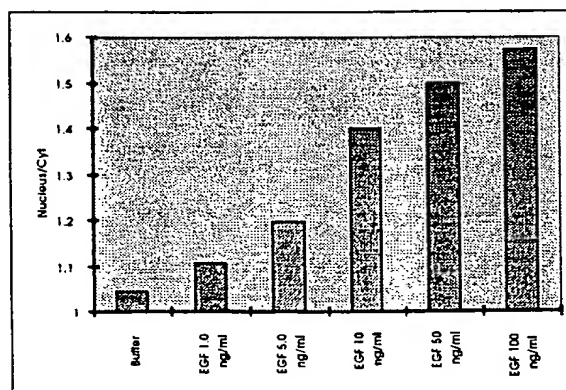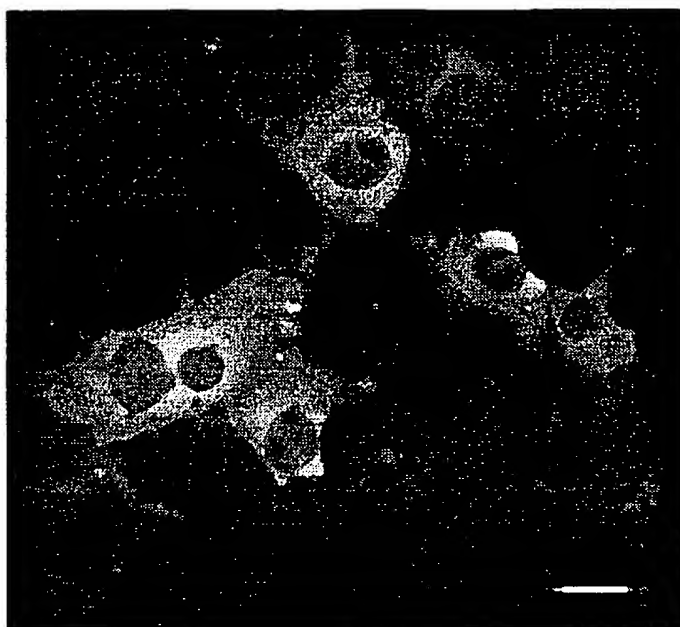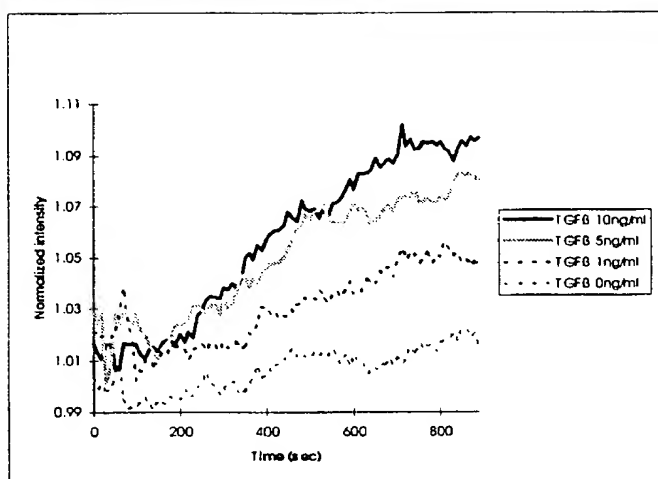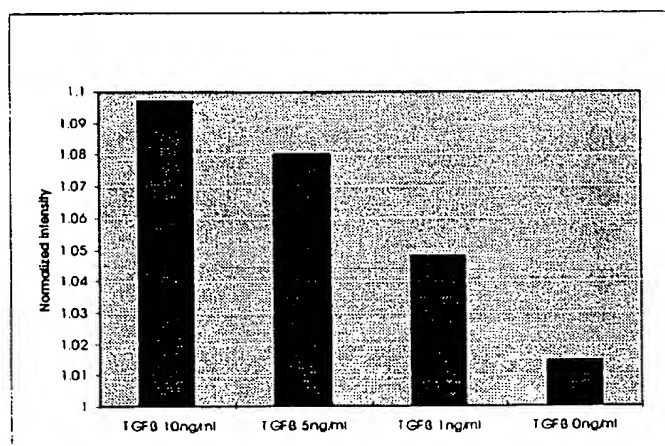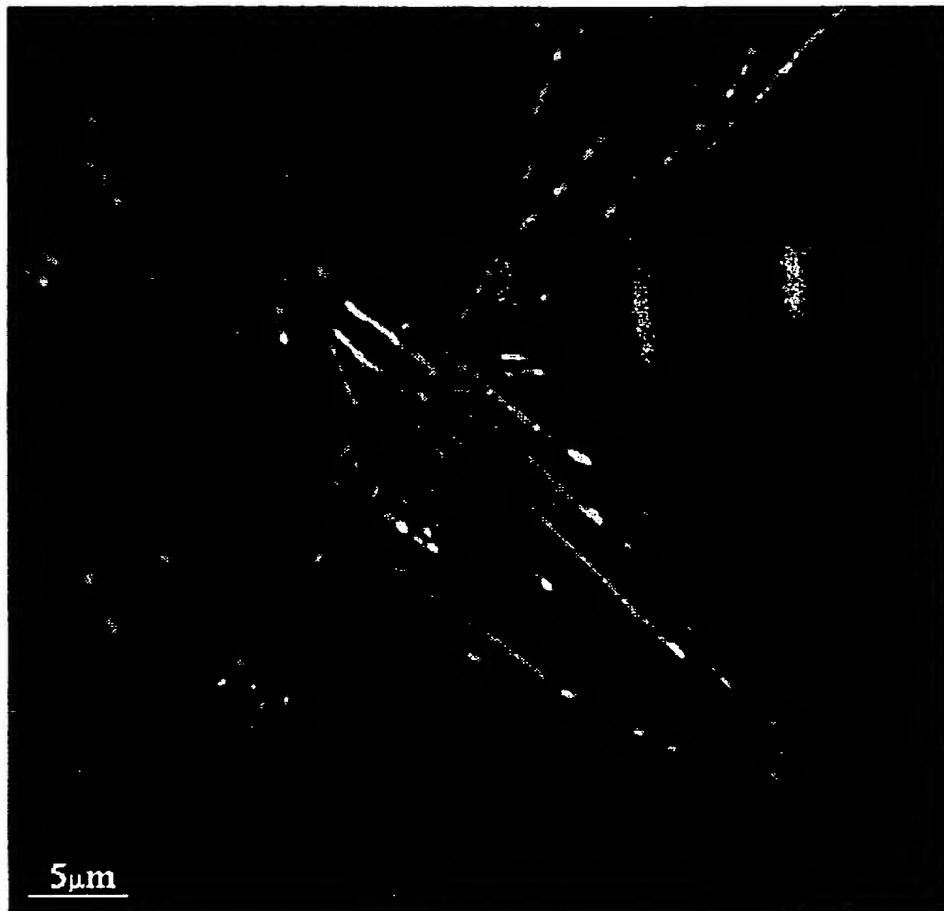
Fig. 12

THIS PAGE BLANK (USPTO)

PCT

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : G01N 33/50, C12Q 1/48, 1/25	A3	(11) International Publication Number: **WO 98/45704** (43) International Publication Date: 15 October 1998 (15.10.98)

(21) International Application Number: PCT/DK98/00145

(22) International Filing Date: 7 April 1998 (07.04.98)

(30) Priority Data:
0392/97   7 April 1997 (07.04.97)   DK

(71) Applicant *(for all designated States except US)*: NOVO NORDISK A/S [DK/DK]; Novo Allé, DK–2880 Bagsvaerd (DK).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: THASTRUP, Ole [DK/DK]; Birkevej 37, DK–3460 Birkerød (DK). PETERSEN BJØRN, Sara [DK/DK]; Klampenborgvej 102, DK–2800 Lyngby (DK). TULLIN, Søren [DK/DK]; Karl Gjellerups Alle 18, DK–2860 Søborg (DK). KASPER, Almholt [DK/DK]; Eigilsgade 32, 4. tv. DK–2300 København S (DK). SCUDDER, Kurt [US/DK]; Lavendelhaven 70, DK–2830 Virum (DK).

(74) Common Representative: NOVO NORDISK A/S; attn. Lars Kellberg, Novo Allé, DK–2880 Bagsværd (DK).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
22 April 1999 (22.04.99)

(54) Title: A METHOD FOR EXTRACTING QUANTITATIVE INFORMATION RELATING TO AN INFLUENCE ON A CELLULAR RESPONSE

(57) Abstract

Cells are genetically modified to expresss a luminophore, e.g., a modified (F64L, S65T, Y66H) Green Fluorescent Protein (GFP, EGFP) coupled to a component of an intracellular signalling pathway such as a transcription factor, a cGMP– or cAMP–dependent protein kinase, a cyclin–, calmodulin– or phospholipid–dependent or mitogen–activated serine/threonin protein kinase, a tyrosine protein kinase, or a protein phosphatase (e.g. PKA, PKC, Erk, Smad, VASP, actin, p38, Jnk1, PKG, IkappaB, CDK2, Grk5, Zap70, p85, protein–tyrosine phosphatase 1C, Stat5, NFAT, NFkappaB, RhoA, PKB). An influence modulates the intracellular signalling pathway in such a way that the luminophore is being redistributed or translocated with the component in living cells in a manner experimentally determined to be correlated to the degree of the influence. Measurement of redistribution is performed by recording of light intensity, fluorescence lifetime, polarization, wavelength shift, resonance energy transfer, or other properties by an apparatus consisting of e.g. a fluorescence microscope and a CCD camera. Data stored as digital images are processed to numbers representing the degree of redistribution. The method can be used as a screening program for identifying a compound that modulates a component and is capable of treating a disease related to the function of the component.

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6   G01N33/50   C12Q1/48   C12Q1/25

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6   G01N   C12Q   C12N   C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 11094 A (NOVONORDISK AS ;THASTRUP OLE (DK); TULLIN SOEREN (DK); POULSEN LAR) 27 March 1997	1-27, 30-40, 44-60, 64-82,88
	see the whole document	
Y	see claims	28,29, 41,61-63

X	WO 91 01305 A (UNIV WALES MEDICINE) 7 February 1991	1-27, 30-40, 42-60, 64-84, 87,88
	see page 4, line 15 - line 20	
Y	see claims	28,29, 41,61-63
	see examples 1-10	

	-/--	

| X | Further documents are listed in the continuation of box C. | X | Patent family members are listed in annex. |

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 January 1999	25. 02. 1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hoekstra, S

9

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category ·	Citation of document, with indication.where appropriate. of the relevant passages	Relevant to claim No.
X	WO 95 07463 A (UNIV COLUMBIA ;WOODS HOLE OCEANOGRAPHIC INST (US); CHALFIE MARTIN) 16 March 1995 cited in the application	1-27, 30-40, 42-60, 64-84, 87,88
	see claim 26	
Y	see the whole document	28,29, 41,61-63

Y	WO 96 23898 A (NOVONORDISK AS ;THASTRUP OLE (DK); TULLIN SOEREN (DK); POULSEN LAR) 8 August 1996 see the whole document	28,29, 41,61-63
X	see page 8-17	42,43, 46,47

X	WO 96 03649 A (UNIV NORTH CAROLINA) 8 February 1996 see page 49: example 6.10	45

P,X	WO 97 20931 A (US HEALTH ;HTUN HAN (US); HAGER GORDON L (US)) 12 June 1997 see claims 41-58	40,44

P,X	WO 97 30074 A (CYTOGEN CORP ;UNIV NORTH CAROLINA (US)) 21 August 1997 see page 57	44

P,X	WO 98 02571 A (TSIEN ROGER Y ;CUBITT ANDREW B (US); UNIV CALIFORNIA (US)) 22 January 1998	1-27, 30-40, 42-50, 52-54, 57-60, 64-82,88
	see claims	

E	WO 98 30715 A (ISACOFF EHUD Y ;SIEGAL MICAH S (US); UNIV CALIFORNIA (US); CALIFOR) 16 July 1998 see the whole document	1-84,87, 88

	-/--	

9

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	SAKAI, N. ET AL.: "Direct visualization of the translocation of the gamma subspecies of protein kinase c in living cells using fusion proteins with green fluorescent protein." THE JOURNAL OF CELL BIOLOGY, vol. 139, no. 6, 15 December 1997, pages 1465-1476, XP002078902 see the whole document	1-43,46, 47,49, 53-57, 59-82,88
O,X	& Direct visualization of the translocation of the gamma subspecies of protein kinase c in living cells using fusion proteins with green fluorescent protein.Meeting held at 22-23.03.97 cited in the application see abstract	

X	SCHMIDT, D.J. ET AL.: "Dynamic analysis of alpha-PKC-GFP chimera translocation events in smooth muscle with ultra-high speed 3D fluorescence microscopy" FASEB JOURNAL, vol. 11, no. 3, 28 February 1997, page A505 XP002077257 cited in the application see abstract	1-43,46, 47,49, 53-57, 59-82,88

X	GERISCH, GUENTHER ET AL: "Chemoattractant-controlled accumulation of coronin at the leading edge of Dictyostelium cells monitored using a green fluorescent protein-coronin fusion protein" CURR. BIOL. (1995), 5(11), 1280-5 CODEN: CUBLE2;ISSN: 0960-9822, XP002089510 see abstract p 1281, right col, second full , last sentence	1,40,43, 45

X	SIDOROVA, JULIA M. ET AL: "Cell cycle-regulated phosphorylation of Swi6 controls its nuclear localization" MOL. BIOL. CELL (1995), 6(12), 1641-58 CODEN: MBCEEV;ISSN: 1059-1524, XP002089512 see the whole document	40,43,44

X	HAN HTUN ET AL: "VISUALIZATION OF GLUCOCORTICOID RECEPTOR TRANSLOCATION AND INTRANUCLEAR ORGANIZATION IN LIVING CELLS WITH A GREEN FLUORESCENT PROTEIN CHIMERA" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 93, no. 10, May 1996, pages 4845-4850, XP002029560 see the whole document	1-40,44, 64-72

9

-/--

INTERNATIONAL SEARCH REPORT

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document. with indication.where appropriate. of the relevant passages	Relevant to claim No.
X	CAREY K L ET AL: "EVIDENCE USING A GREEN FLUORESCENT PROTEIN-GLUCOCORTICOID RECEPTOR CHIMERA THAT THE RAN/TC4 GTPASE MEDIATES AN ESSENTIAL FUNCTION INDEPENDENT OF NUCLEAR PROTEIN IMPORT" THE JOURNAL OF CELL BIOLOGY, vol. 133, no. 5, June 1996, pages 985-996, XP000670316 cited in the application see the whole document	1-40,44, 64-72
X	OGAWA H ET AL: "LOCALIZATION, TRAFFICKING, AND TEMPERATURE-DEPENDENCE OF THE AEQUOREA GREEN FLUORESCENT PROTEIN IN CULTURES VERTEBRATE CELLS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 92. no. 25, 5 December 1995, pages 11899-11903, XP002029556 see the whole document	1-40,44, 64-72
X	WESTPHAL, MONIKA ET AL: "Microfilament dynamics during cell movement and chemotaxis monitored using a GFP - actin fusion protein" CURR. BIOL. (1997), 7(3), 176-183 CODEN: CUBLE2;ISSN: 0960-9822, XP002090291 see page 181, left-hand column, line 1	1,40,43, 45
X	TODA, TAKASHI ET AL: "The fission yeast sts5+ gene is required for maintenance of growth polarity and functionally interacts with protein kinase C and an osmosensing MAP kinase pathway" J. CELL SCI. (1996), 109(9), 2331-2342 CODEN: JNCSAI;ISSN: 0021-9533, XP002090292 see abstract	40,42
A	WEBB, CHRIS D. ET AL: "Use of green fluorescent protein for visualization of cell-specific gene expression and subcellular protein localization during sporulation in Bacillus subtilis" J. BACTERIOL. (1995), 177(20), 5906-11 CODEN: JOBAAY;ISSN: 0021-9193, XP002089513 see the whole document	44
A	WO 94 23039 A (CANCER RES INST ROYAL ;MARSHALL CHRISTOPHER JOHN (GB); ASHWORTH AL) 13 October 1994 see the whole document	1-84,87, 88

9

INTERNATIONAL SEARCH REPORT

Box I   Observations where certain claims wer found un earchabl (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 83-84 and claim 87 relate to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition (Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy).

2. [X] Claims Nos.:   85,86
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II   Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest   [X] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1992)

FURTHER INFORMATION CONTINUED FROM   PCT/ISA/ 210

Claims Nos.: 85,86

The subject-matter (compounds per se) is solely characterised in claims
85 and 86 by the result to be achieved, no support of a technical
character is derivable from the description for the technical formulation
of the subject of the search, accordingly no scope of a search could be
defined and a meaningfull search is hence not possible.

FURTHER INFORMATION CONTINUED FROM   PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Partially: 1-43, 46, 59-82 and 88; Entirely: 47, 49, 53-57

> Methods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being serine/threonine protein kinases

2. Claims: Partially: 1-41, 43, 59-82 and 88; Entirely: 48

> Methods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being to tyrosine kinases

3. Claims: Partially: 1-43, 46, 59-82 and 88; Entirely: 50, 51

> MMethods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being to cAMP dependent protein kinases.

4. Claims: Partially: 1-43, 46, 59-82 and 88; Entirely: 52

> MMethods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active

page 1 of 2

FURTHER INFORMATION CONTINUED FROM   PCT/ISA/ 210

molecule, in particular to a molecule involved in
intracellular signalling pathways, nucleic acids encoding
fusion proteins comprising bothe the luminophore and the
biological active molecule, cells containing and expressing
these nucleic acids, as well as methods and apparatuses
involving above products, inso far as related to the
biologically active protein being cGMP dependent protein
kinases

5. Claims: Partially: 1-43, 59-82 and 88; Entirely: 58

Methods for extracting information from influences on a
living cell involving observing spatial redistribution or
modulation of a luminophore linked to a biologically active
molecule, in particular to a molecule involved in
intracellular signalling pathways, nucleic acids encoding
fusion proteins comprising bothe the luminophore and the
biological active molecule, cells containing and expressing
these nucleic acids, as well as methods and apparatuses
involving above products, inso far as related to the
biologically active protein being protein phosphatases

6. Claims: Partially: 1-41, 43, 59-82 and 88; Entirely: 44

Methods for extracting information from influences on a
living cell involving observing spatial redistribution or
modulation of a luminophore linked to a biologically active
molecule, in particular to a molecule involved in
intracellular signalling pathways, nucleic acids encoding
fusion proteins comprising bothe the luminophore and the
biological active molecule, cells containing and expressing
these nucleic acids, as well as methods and apparatuses
involving above products, inso far as related to the
biologically active protein being to transcription factors

7. Claims: Partially: 1-41, 43, 59-82 and 88; Entirely: 45

Methods for extracting information from influences on a
living cell involving observing spatial redistribution or
modulation of a luminophore linked to a biologically active
molecule, in particular to a molecule involved in
intracellular signalling pathways, nucleic acids encoding
fusion proteins comprising bothe the luminophore and the
biological active molecule, cells containing and expressing
these nucleic acids, as well as methods and apparatuses
involving above products, inso far as related to the
biologically active protein being to proteins associated
with the cytoskeletal network

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9711094	A	27-03-1997	AU	4482996 A	09-04-1997
			CA	2232727 A	27-03-1997
			EP	0851874 A	08-07-1998
WO 9101305	A	07-02-1991	AU	6054590 A	22-02-1991
			CA	2064766 A	23-01-1991
			EP	0484369 A	13-05-1992
			JP	5501862 T	08-04-1993
			US	5683888 A	04-11-1997
WO 9507463	A	16-03-1995	US	5491084 A	13-02-1996
			AU	694745 B	30-07-1998
			AU	7795794 A	27-03-1995
			CA	2169298 A	16-03-1995
			EP	0759170 A	26-02-1997
			JP	9505981 T	17-06-1997
WO 9623898	A	08-08-1996	AU	4483096 A	21-08-1996
			CA	2217700 A	08-08-1996
			EP	0815257 A	07-01-1998
WO 9603649	A	08-02-1996	AU	3146095 A	22-02-1996
			CA	2195629 A	08-02-1996
			EP	0772773 A	14-05-1997
			JP	10503369 T	31-03-1998
WO 9720931	A	12-06-1997	AU	1283497 A	27-06-1997
			CA	2239951 A	12-06-1997
WO 9730074	A	21-08-1997	AU	2272397 A	02-09-1997
WO 9802571	A	22-01-1998	AU	3801997 A	09-02-1998
WO 9830715	A	16-07-1998	AU	5090498 A	03-08-1998
WO 9423039	A	13-10-1994	AU	677834 B	08-05-1997
			AU	6382394 A	24-10-1994
			EP	0703984 A	03-04-1996
			JP	9501302 T	10-02-1997
			AU	696939 B	24-09-1998
			AU	1586195 A	29-08-1995
			CA	2182967 A	17-08-1995
			EP	0742827 A	20-11-1996
			WO	9521923 A	17-08-1995
			JP	9508795 T	09-09-1997